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Case Report

A Giant Malignant Melanoma Presenting as Submandibular Lump: A Case Report

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Abstract

Malignant melanoma with its varied clinical presentations and histomorphological patterns is a perplexing problem. We hereby report a case of malignant melanoma presenting as submandibular lump in 80-year-old female since 6 months and was rapidly increasing in size. On cytology, it was diagnosed as malignant melanoma.

Key words: Malignant melanoma, submandibular lump, head and neck

INTRODUCTION

Melanoma is a malignant tumor produced from malignant transformation of melanocytes. This can be sporadic or arise from a pre-existing premalignant lesion. As melanocytes are of neural crest origin, they can arise in other locations where neural crest cells are present, including the brain and gastrointestinal tract.[1] Approximately 10–25% of melanomas are found in the head and neck region and majority of them (85–90%) are cutaneous lesions, most often arising in the skin of face.[2] In 2019, this type of malignancy was the third most frequent cancer to be diagnosed in males and the fifth most in females according to the American Cancer Society and the National Cancer Institute.[3] Malignant melanoma with its various clinical presentations and histomorphological patterns is a perplexing problem both for the diagnosticians and clinicians. We hereby report a case of malignant melanoma presenting as a submandibular lump in 80 year old female. This lump was present for 6 months and was rapidly increasing in size.

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CASE DESCRIPTION

A 80-year-old female presented to ENT outpatient department of our hospital with a mass in the left submandibular region for 6 months which was rapidly increasing in size. On clinical examination, there was a large mass measuring 4*4 cm in size in the left submandibular region which was non-tender, fungating with involvement of the skin [Figure 1]. It was foul smelling with presence of black crusting and oozing of blood. Bilateral level 1, 2, and 3 lymph nodes were involved. Fine-needle aspiration cytology from this mass yielded positive for malignant cells.

Biopsy was taken from the mass and on microscopic examination that it showed extensive ulceration and focal parts of tumor arranged in form of sheets of oval to spindle shaped tumor cells having hyperchromatic nuclei, visible nucleoli, and moderate cell cytoplasm. Areas of intracellular pigment deposition noted.

Meanwhile contrast-enhanced computed tomography was done which showed a well-defined heterodense enhancing lesion in the left submandibular region approximately 44*42*41 mm suggesting possibility of neoplastic etiology. Further, 18 fluorodeoxyglucose positron emission tomography computed tomograph showed metabolically active large ill-defined heterogeneously enhancing soft-tissue density lesion in the left submandibular region. The lesion was involving the overlying skin and no calcification

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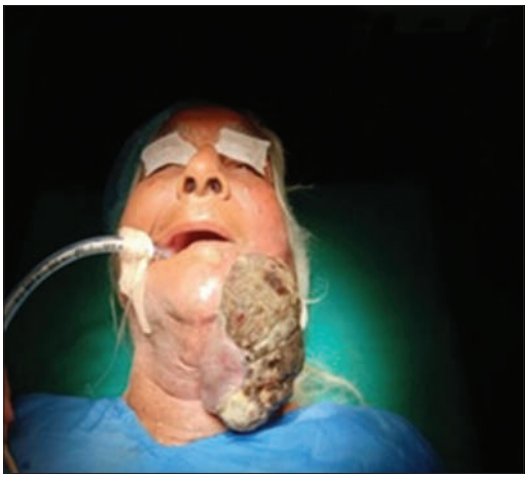

Figure 1: A large mass measuring 4*4 cm in size in the left submandibular region with fungating involvement

noted within the lesion. Few hypodense areas suggestive of necrosis noted within the mass lesion abutting left ramus of mandible with no obvious erosion.

Considering the site and morphology, a diagnosis of malignant melanoma was considered and an urgent excision was advised. The patient was taken up for the surgery, and intraoperatively, the mass was found involving the overlying dermis only. However, the submandibular salivary gland was not related to the mass. The mass was excised and sent for histopathological examination. Hematoxylin and eosin stained sections showed malignant tumor arranged in sheets. The individual tumor cells have oval to spindle shaped nuclei, vesicular nuclear chromatin, prominent nucleoli, and moderate amount of cytoplasm. Few of the tumor cells exhibit melanin pigment in the cytoplasm [Figure 2]. In view of these findings, final diagnosis of malignant melanoma was made.

DISCUSSION

Metastatic melanoma with its variable morphological features is a great histopathological mimicker and may be confused with tumors of nearly all lineages. Various superficial soft-tissue tumors with epithelioid and/or spindle cells or with pigment can mimic it. The prevalence of solitary lesions of melanoma confined to dermal or subcutaneous tissue has been reported to be 0.51%, 0.63%, and 0.92% in three large series.[4,5] The sites included are the head and neck, upper extremity, lower extremity, and trunk.

Clinically, lesions are classified according to their depth, as follows:

- Thin – 1 mm or less
- Moderate – 1 mm to 4 mm
- Thick – >4 mm

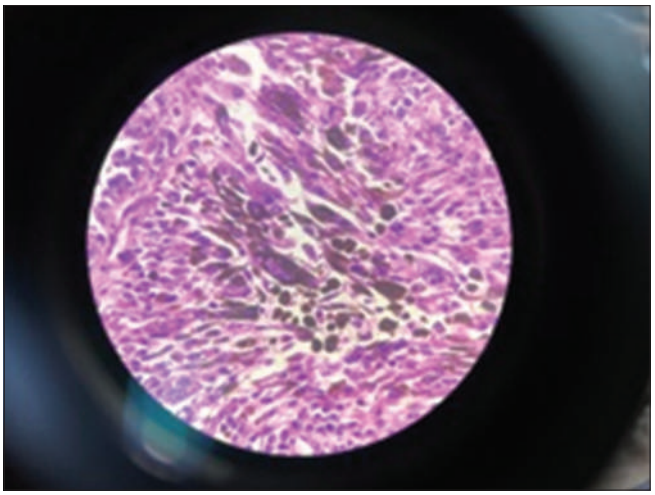

Figure 2: Histopathological slide image showing malignant tumor arranged in sheets having oral to spindle shaped nuclei, vesicular nuclear chromatin, prominent nucleoli, and few of the tumor cells exhibit melanin pigment in the cytoplasm

According to the growth pattern, there are four major types of melanoma:

- Superficial spreading melanoma constitutes approximately 70% of melanomas, usually flat but may become irregular and elevated in later stages; the lesions average 2 cm in diameter, with variegated colors, as well as peripheral notches, indentations, or both
- Nodular melanoma accounts for approximately 15–30% of melanoma diagnoses; the tumors typically are blue-black but may lack pigment in some circumstances
- Lentigo maligna melanoma represents 4–10% of melanomas; the tumors are often larger than 3 cm, flat and tan, with marked notching of the borders
- Acral lentiginous melanoma constitutes 2–8% of melanomas; may appear on the palms and soles as flat, tan or brown stains with irregular borders.[6]

Classically, melanoma lesions have been staged according to the Clark staging system, a description of the histologic level of invasion and the Breslow staging system, and a measure of the absolute depth of the lesion [Table 1].[7,8]

With the adoption of American Joint Committee on Cancer TNM staging system, the definition of nodal staging has become increasingly important. 10–30% of melanoma patients present with clinically detectable cervical metastases.[9]

In our case, the depth was <1.5 mm and it was classified under II category.

The preferred method of tissue sampling for the diagnosis of melanoma is excisional biopsy with a margin of normal tissue measuring at least 2 mm.

Table 1: Clark and Breslow staging systems

Clark	Breslow
Confined to epidermis	I<0.75 mm
Invading papillary dermis	II 0.76–1.5 mm
Abutting papillary-reticular junction	III 1.51–4.0 mm
Invading reticular dermis	IV>4.0 mm
Subcutaneous invasion	V —

Surgery such as wide local excision with sentinel lymph node biopsy, elective node dissection, or both is the definitive treatment for early-stage melanoma. When performing the wide local excision, first consider the surgical margins. If the primary closure is not feasible, skin grafting or tissue transfers may be needed.[10] Medical management is reserved for adjuvant therapy of patients with advanced melanoma.

CONCLUSION

Malignant melanoma with its varied clinical presentations and histomorphological patterns is a perplexing problem. Malignant melanoma is a difficult diagnosis to make particularly when the primary site is not known. Since it is an aggressive tumor, the importance of timely diagnosis is unquestionable.

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We confirm that this manuscript has not been published elsewhere and is not under consideration by another journal. All the authors have approved the manuscript and agreed to the submission.

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Original Article

Role of Cytochemical and Morphological Analysis in the Field of Oncopathology for the Evaluation of Acute Leukemia in the Modern Era of Flowcytometry: A Study Done in a Tertiary Care Hospital in Northern India

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Abstract

Introduction: Hematopoiesis is a complex developmental process whereby multiple cell lineages residing in the bone marrow (BM), peripheral blood and lymphatic organs, undergo differentiation, and proliferation.

Material & Methods: This study was conducted on 50 cases of Acute Leukemia in the department of pathology, Sri Guru Ramdas Institute of Medical Sciences and Research, Amritsar. It is a cross sectional, laboratory-based and observational study. BM aspiration and biopsy was performed on the cases and the slides prepared from the BM aspirate as well as peripheral blood film were subjected to morphological analysis and cytochemical staining including MPO, SBB, PAS, and NSE stains.

Results: The results are depicted in tables. It was observed that males overall showed a higher no. of cases of acute leukemia as compared to females.

Conclusion: Flowcytometric immunophenotyping has a clear correlation with prognosis and, in an era where novel agents are being developed, may assist in the production of monoclonal antibodies that are specific to tumor antigens. Flow cytometry is the gold standard for evaluating minimal residual illness, particularly in instances when there is no clear molecular signature

Key words: Acute Leukemia, Flowcytometry, Oncopathology

INTRODUCTION

Hematopoiesis is a complex developmental process whereby multiple cell lineages residing in the bone marrow (BM), peripheral blood and lymphatic organs, undergo differentiation, and proliferation. These cells originate from a small number of stem cells with self-renewing potential, which give rise to a mixture of cells with different levels of maturation. Many of these cell types can be identified using lineage-specific and differentiation-specific antibodies. Leukemia results from the proliferation of a clone of abnormal hematopoietic cells with impaired differentiation, regulation, and programmed cell death (apoptosis).[1]

Myeloid or lymphoid leukemia is caused by malignant growth in the cell lineage of myeloid or lymphoid cells. The sick cells amass, cease differentiating, and finally stop maturing, preventing the growth of healthy progenitor cells. Compared to acute leukemia, when lineage proliferation is stopped at an early stage of differentiation and results in a very aggressive, rapidly spreading illness, chronic leukemia has a longer course of development and blocks cell maturation at a later stage.[2,3]

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Four main leukemia kinds are recognized based on these two key distinctions, myeloid or lymphoid and chronic or acute: Acute myeloid leukemia (AML), acute lymphoid leukemia (ALL), chronic myeloid leukemia, and chronic lymphoid leukemia. Each type has a distinctive shape, and diagnosis is made through cytological microscopic evaluation of BM smears or peripheral blood smears and histological examination of each patient's BM biopsy.[3,4]

Acute leukemias are the result of accumulation of early myeloid or lymphoid precursors in the BM, blood and other tissues and are thought to arise by somatic mutation of a single cell within a minor population of stem or early progenitor cells in the BM or thymus. As per the World Health Organization, classification a blast count of above 20% is sufficient for the diagnosis of acute leukemia as against 30% blasts prescribed earlier.[5]

Acute leukemia is a rapidly progressing disease that affects red and white blood cells and platelets that are not yet fully developed, meaning these cells cannot carry out their normal functions. This type of leukemia is divided into two categories, depending on the cell type involved. If the disease involves the lymphocytes it is called ALL, but if it affects the myeloid cells it is known as AML.[5]

The diagnosis of acute leukemia entails a stepwise approach. First in sequence and importance is the distinction of acute leukemia from other neoplastic diseases and reactive disorders. Second is differentiating AML and ALL. The third facet is the classification of AML and ALL into categories that define treatment and prognostic groups. Continued development of second-generation tyrosine kinase inhibitors and the emergence of immunotherapy, including blinatumomab and chimeric antigen receptor T-cell therapy, have improved survival.[6]

A peripheral blood smear and BM aspiration should be examined and correlated with the results of a complete blood count. Leishman stain is used to color BM aspirates (BMA) and peripheral blood smears. Hematoxylin and eosin and reticulin stain are used to color the BM samples that were taken. In biopsy cases that presented diagnostic challenges, relevant immunohistochemical stains such as anti-Myeloperoxidase (MPO) and CD34 are used.[6,7]

Because earlier precursors of several cell series have a striking degree of resemblance, it can be challenging to morphologically identify cells in AL. The morphologic characteristics in instances of poorly differentiated AL may be ambiguous, necessitating more research. When there is an asynchronism between nuclear and cytoplasmic maturation, cytochemical stains are very helpful in identifying the kind of precursor cells. Early precursors that include such cytochemically stainable components are easier to identify since they are undergoing specialized cellular differentiation, which is indicated by their existence. The most used tests are MPO and Periodic acid Schiff (PAS), which are useful in separating AML from ALL. Different leukemia types showed distinctive cytochemical patterns. Blasts that are MPO positive are very specific for AML.[8]

ALL exhibits PAS block positive, which is significant given the absence of Sudan Black B (SBB) positivity. It makes no difference if PAS positive is diffuse or granular. Most instances of acute leukemia may be correctly classified as AML or ALL according to FAB classification by adding cytochemistry to the morphologic evaluation. There are still a small number of situations, nevertheless, when these techniques cannot provide a firm diagnosis. Since the blastic cells in these situations are fully undifferentiated and lack the full complement of enzymes and metabolic products, cytochemistry cannot help with the diagnosis.[9]

Despite the fact that FCM is more widely used, it has drawbacks such as the difficulty in interpreting borderline positive, the lack of blasts in dry tap BMA, and the strict requirements for fresh sample. As a result, the only source currently accessible for the diagnosis and categorization of acute leukemia is the value of IHC.[10-12] However, the sensitivity of these approaches for the detection of MPO to diagnose AML has not been consistently reported in the literature. This is especially significant at a time when cytochemistry and IHC are losing their relevance.[13,14]

Immunophenotyping may successfully identify the lineage of the majority of morphologically and cytochemically poorly differentiated AL patients. AML and ALL immunophenotypic subgroups can also be identified.[15,16] For immunophenotyping AL, multiparametric flow cytometry is the technique of choice. The immunophenotypic categories are crucial for ALLs because they distinguish between different prognosis and therapy groups. Immunophenotyping is crucial for separating poorly differentiated cases from ALL in AMLs.[17]

Among AL, aberrant phenotypes are characterized by antigen expression patterns on malignant cells that deviate from the course of typical hematological development. Lineage infidelity (lymphoid marker expression in myeloid blast cells such as CD7, CD19, CD79a, CD10, CD2, CD5, and CD3 expression) and asynchronous antigen expression (coexistence of early and late markers in one cell such as CD34 and CD15 in AML) are two examples of aberrant antigen expression in AL. Aside from lineage-specific antigens, which are absent when expected antigen expression is absent, other examples of aberrant expression include antigen overexpression, which is the

abnormally increased expression of a particular antigen per cell, aberrant light scatter properties, and antigen absence (CD13 and CD33 on myeloid blasts). Cross-lineage antigen expression, such as that of myeloid antigens in ALL, T-lineage antigens in T-ALL, or B-lineage antigens in B-ALL, is one of these aberrancies.[18-22]

Due to the paucity of literature in relation to our study population. The present study was done for the comparison of Morphological, Cytochemical, and Flow Cytometric diagnosis in Acute Leukemia.

MATERIAL AND METHODS

This study was conducted on 50 cases of Acute Leukemia in the department of pathology, Sri Guru Ramdas Institute of Medical Sciences and Research, Amritsar. It is a cross-sectional, laboratory-based and observational study. BM aspiration and biopsy was performed on the cases and the slides prepared from the BM aspirate as well as peripheral blood film were subjected to morphological analysis and cytochemical staining including MPO, SBB, PAS, and NSE stains. All the cases were the sent subjected to flowcytometry and evaluated.

Materials

List of cytochemical stains to be used:

- MPO.
- SBB.
- Reaction PAS.
- Esterases
    - Naphthol AS-D Chloroacetate Esterase
    - Naphthyl Butyrate Esterase (ANBE)

MPO

Procedure

Reagents:

- Fixative-Buffered Formal Acetone (BFE)
- Acetone-40 mL
- Buffer- 30 mL
- Formalin-25 mL

Substrate-3,3'-Diaminobenzidine (DAB)

Buffer-Sorensen's phosphate buffer, PH-7.3

- Hydrogen peroxide (H2O2, 30% w/v)
- Counterstain-Aqueous hematoxylin

Staining method

- Fix air dried smears in cold buffered acetone for 30 s.
- Rinse in running tap water and dry.
- Incubate for 10 min. in working substrate solution. (working substrate solution 30 mg of DAB in 60 mL buffer, and add 120 μL H202 just before use.)
- Wash, counter stain with hematoxylin for 3–5 min.
- Rinse in running tap water and air dry.

Interpretation

- Early myeloblasts are negative, with granular positivity appearing progressively as they mature.
- Dark brown granules in the cytoplasm of granulocytes and monocytes.
- Monocytes exhibit weaker and more scattered staining properties than granulocytes.
- Eosinophil granules stain strongly.
- Plasma cells and lymphoblast are negative.
- Neutrophilic granules stain positive for MPO, hence used as a positive control.

SBB

Preparation

- Reagent stain SBB 0.3 g powder is dissolved in 100 ml of absolute ethanol, to make a solution.
- Phenol buffer is prepared by dissolving 16 g of crystalline phenol in 30 ml of absolute ethanol. This is added with 100 ml of distilled water, in which 0.3 of Disodium phosphate is dissolved.
- Working stain solution is made by adding 40 ml of phenol buffer with 60 ml of Sudan Black prepared solution.

Staining method

- Fix the air-dried blood smears with formalin vapor in a coplin jar, after this air wash the slides for 15 min.
- Immerse the smear slide in the working SBB stain solution for 1 h in a coplin jar, closed with a lid.
- After 1 h, place the slide on a staining rack, and flood the slides with 70% alcohol, after 30 s, tip off the alcohol, and flood again with 70% alcohol for 30 s. Repeat the flooding 3 times.
- Rinse the smear with running tap water and air dry.
- Counterstain the slide with Leishman stain or May-Grunwald-Giemsa stain.

Interpretation

- The results are similar to MPO staining both in normal and leukemic cells.
- The difference is that the eosinophil granules are SBB negative.
- In rare cases of ALL, non granular smudgy positivity is not seen in MPO staining eg. In Burkett's lymphoma.
- SBB positive prominent Auer rods in BM smear.

Periodic PAS

Preparation

Reagents

- Fixative-methanol
- 1% periodic acid (HIO4)

- Schiff's reagent
- Counter stain-aqueous hematoxylin

Staining method

- Fix films for 15 min. in methanol.
- Rinse in running tap water and air dry.
- Treat slides with 1% periodic acid for 10 min.
- Rinse in running tap water for 10 min. and air dry
- Now treat with Schiff's reagent for 30 min.
- Rinse in running tap water and air dry.
- Counterstain with aqueous hematoxylin for 5 min. then wash and air dry.

Results

- The reaction product is red.
- Cytoplasmic positivity may be diffuse or granular

Interpretation

- Granular precursors show diffuse weak positivity with neutrophils showing intense granular positivity and act as internal positive controls
- Eosinophil granules are negative with diffuse cytoplasmic positivity
- Basophils are negative
- Monocytes and their precursors show variable diffuse positivity
- Normal erythroid precursors and RBC's are negative. But dysplastic erythroblast are positive
- Megakaryocytes and platelets are positive
- Lymphoblasts show PAS blocks or granules i.e. block positivity
- Myeloblasts are negative for this stain

α-ANBE

Preparation

Retxgent:

- Fixative-BFE.
- Buffer-66 mmol/l phosphate buffer, ph 7.4
- Substrate-α-naphthyl butyrate
- Coupling reagent-Fast garnet GBC
- Counterstain-aqueous hematoxylin

Staining method

- Counterstain with aqueous hematoxylin for 1 min
- Fix air dried smears in cold BFEbuffered formal acetone for 30 s
- Rinse gently in running tap water and air dry
- Rinse in running tap water and air dry
- Rinse in running tap water and air dry
- Treat the slides with substrate solution for 5–10 min

Interpretation

- The majority of monocytes (>80%) stain strongly.
- Granulocytes and platelets are negative.
- B-lymphocytes are negative but T-lymphocytes are positive.

ANBE is more specific for identifying the monocytic component in AML.

RESULTS

This study was conducted on Acute Leukemia cases collected from April 2021 to July 2022, which have been proven to have cells of premature lineage on microscopy, by employing morphological and cytochemical methods of staining and hence diagnosed in the Department of Pathology, Sri Guru Ram Das Institute Of Medical Sciences And Research, Amritsar and comparing it with the flowcytometric results of those cases. The observations and the results deduced were as follows.

The observed cases were in the range of 1–85 years. Table 1 shows the age distribution, with the majority of the percentage lying in the age group 1–20 years and 21–40 years, each having 14 cases in the category, which was found to be 28% each, hence totaling to 56%. This was followed by the age group 41–60 years, with 13 cases, which was 16%, and 61 to 80 years group with 8 cases having 16%, followed by the more than 80 years group with only 1 case, amounting to 2%.

Table 1: Age distribution of patients

Age (years)	Number of cases, *n* (%)
1–20	14 (28.0)
21–40	14 (28.0)
41–60	13 (26.0)
61–80	8 (16.0)
>80	1 (2.0)
Total	50 (100)

Table 2: Age distribution of leukemia cases

Age	ALL, *n* (%)	AML, *n* (%)	Total	χ^2	*P*-value
1–20	11 (78.6)	3 (21.4)	14	18.47	<0.001
21–40	5 (35.7)	9 (64.3)	14		
41–60	2 (15.4)	11 (84.6)	13		
61–80	0	8 (100.0)	8		
>80	0	1 (100.0)	1		

ALL: Acute lymphoid leukemia, AML: Acute myeloid leukemia

Table 3: Sex distribution of cases

Sex	Number of patients, *n* (%)
Female	23 (46.0)
Male	27 (54.0)
Total	50 (100.0)

Total no. of Male patients-27 i.e., 54.0%, Total no. of Female patients-23 i.e., 46.0%

Table 4: Sex distribution in cases of acute lymphoid leukaemia and acute myeloid leukaemia

Sex	ALL, *n* (%)	AML, *n* (%)	Total	χ^2	*P*-value
Female	6 (26.1)	17 (73.9)	23	1.817	0.178
Male	12 (44.4)	15 (55.6)	27		

ALL: Acute lymphoid leukemia, AML: Acute myeloid leukemia

Table 5: Distribution of patients according to types and sub types of leukemia

Diagnosis	ALL, *n* (%)	AML, *n* (%)	Total	χ^2	*P*-value
ALL	5 (100.0)	0	5	50.000	<0.001
ALL (hepatosplenic lymphoma)	1 (100.0)	0	1		
AML	0	23 (100.0)	23		
AML M0	0	1 (100.0)	1		
AML-M1	0	2 (100.0)	2		
AML-M3	0	3 (100.0)	3		
APML – hypergranular variant	0	1 (100.0)	1		
B-ALL	11 (100.0)	0	11		
CML (blast crisis)	0	2 (100.0)	2		
T-ALL	1 (100.0)	0	1		

ALL: Acute lymphoid leukemia, AML: Acute myeloid leukemia, CML: Chronic myeloid leukemia, APML: Acute promyelocytic leukaemia , B-ALL: B-Acute Lymphoblastic Leukemia, T-ALL: T-cell acute lymphoblastic leukemia

Table 6: Hemoglobin distribution among the cases

Hb g (%)	ALL, *n* (%)	AML, *n* (%)	Total	χ^2	*P*-value
<6	4 (33.3)	8 (66.7)	12	0.415	0.936
6.1–9	8 (36.4)	14 (63.6)	22		
9.1–12	4 (33.3)	8 (66.7)	12		
12 and above	2 (50.0)	2 (50.0)	4		

ALL: Acute lymphoid leukemia, AML: Acute myeloid leukemia, Hb: Hemoglobin

Table 7: Total leukocyte count in cases

TLC	ALL, *n* (%)	AML, *n* (%)	Total	χ^2	*P*-value
<4000	4 (66.7)	2 (33.30	6	8.76	0.118
4001–11,000	4 (44.4)	5 (55.6)	9		
11,001–50,000	8 (44.4)	10 (55.6)	18		
50,001–100,000	1 (16.7)	5 (83.3	6		
100,001–200,000	0 (0.0)	8 (100.0)	8		
>200,000	1 (33.3)	2 (66.7)	3		

TLC: Total lung capacity, ALL: Acute lymphoid leukemia, AML: Acute myeloid leukemia

Table 8: Platelet count in cases

Platelet count/cu mm	ALL, *n* (%)	AML, *n* (%)	Total	χ^2	*P*-value
<50,000	6 (27.3)	16 (72.7)	22	4.06	0.203
50,000–1 Lac	4 (33.3)	8 (66.7)	12		
1 Lac–1.5 Lacs	0	2 (100.0)	2		
>1.5 Lacs	8 (57.1)	6 (42.9)	14		

ALL: Acute lymphoid leukemia, AML: Acute myeloid leukemia

Table 9: Cytochemical stain MPO

MPO	*n* (%)
Negative	20 (40.0)
Positive	30 (60.0)
Total	50 (100.0)

MPO: Myeloperoxidase

Table 10: Cytochemical stain MPO

MPO	ALL, *n* (%)	AML, *n* (%)	Total	χ^2	*P*-value
Negative	18 (90.0)	2 (10.0)	20	42.188	<0.001
Positive	0	30 (100.0)	30		

ALL: Acute lymphoid leukemia, AML: Acute myeloid leukemia, MPO: Myeloperoxidase

Table 11: Cytochemical stain periodic acid Schiff

PAS	*n* (%)
Negative	33 (66.0)
Positive	17 (34.0)
Total	50 (100.0)

PAS: Periodic acid Schiff

Table 12: Cytochemical stain periodic acid Schiff

PAS	ALL, *n* (%)	AML, *n* (%)	Total	χ^2	*P*-value
Negative	2 (6.1)	31 (93.9)	33	37.813	<0.001
Positive	16 (94.1)	1 (5.9)	17		

ALL: Acute lymphoid leukemia, AML: Acute myeloid leukemia, PAS: Periodic acid Schiff

Table 13: Cytochemical stain Sudan black B

SBB	*n* (%)
Negative	26 (52.0)
Positive	24 (48.0)
Total	50 (100.00)

SBB: Sudan black B

Table 14: Cytochemical stain Sudan black B

SBB	ALL, *n* (%)	AML, *n* (%)	Total	χ^2	*P*-value
Negative	18 (69.2)	8 (30.8)	26	25.962	<0.001
Positive	0	24 (100.0)	24		

ALL: Acute lymphoid leukemia, AML: Acute myeloid leukemia, SBB: Sudan black B

Table 15: Cytochemical stain non-specific esterase

NSE	ALL, *n* (%)	AML, *n* (%)
Negative	18 (100.0)	32 (100.0)
Positive	0	0

ALL: Acute lymphoid leukemia, AML: Acute myeloid leukemia, NSE: Neuron-specific enolase

Table 2 shows, the age distribution for the diagnosed cases, where ALL is common in the age group of 1–20 constituting 11 cases out of the 18 diagnosed cases. Followed by AML, in the age group of with 41–60 years constituting 11 cases out of the diagnosed 32 cases. As seen most of the ALL cases were seen in the younger population, whereas AML was seen mostly in the middle age groups with lesser frequency in the extreme age groups.

It was observed that males overall showed a higher no. of cases of acute leukemia as compared to females. Whereas, the prevalence of AML was seen slightly higher in females as compared to males which showed that out of the total 32 cases of AML, 17 were seen in females and 15 were seen in males. In the total 18 diagnosed cases of ALL, the ratio of occurrence in males to females was 2:1.

This table depicts the distributive nature of the different types and subtypes of leukemia.

Hemoglobin was seen to be lower in cases of AML with 22 cases out of 32 having Hb less than 9 g% with the majority of them lying in the range of 6.1 to 9 g%. Similarly, the majority of ALL cases had their Hb between 6.1 and 9 g% accounting up to 8 cases out of the 18 cases.

Total leukocyte count was seen higher in cases of AML as compared to ALL. The majority of cases were seen to have their TLC between 11001 and 50000, out of which 55.6% were cases diagnosed as AML and 44.4% cases were those of ALL. Hyperleukocytosis was observed in 13 cases, out of which 8 cases of AML had their TLC between 1 lakh to 2 lakh, 1 case of ALL and 2 cases of AML had their TLC more than 2 lakh.

Platelet count was seen to be reduced in most of the cases of AML with almost 26 out of 32 cases and 10 out of 18 cases of ALL had their platelet count <1.5 lakh/cumm. Among the least category of <50000/cumm, 72.7% cases were those of AML and 27.3% cases were those of ALL.

As the table depicts, out of all the suspected cases of acute leukemia, 60% cases were MPO positive.

All the MPO positive cases, turned out to be of AML series, whereas, out of all the MPO negative cases, 90% were later proven to be ALL and 10% proved to be AML. A significant p value was obtained in this relation.

PAS positivity was observed in 17 out of 50 cases, accounting up to 34% of all the cases taken.

Out of all the PAS positive cases, 94.1% were proven to be those of ALL, and 5.9% proved to be AML on flowcytometry. PAS negative cases comprised of predominantly AML cases, that is, 93.9% and 6.1% cases were proven to be those of ALL. Significant p value was obtained in this relation.

On SBB stain out of 50 cases, 48% of them showed SBB positivity.

24 out of the total 50 cases (48%) were SBB positive. Out of the remaining 26 cases which were SBB negative, 30.8% of them later proved to be AML whereas the rest, that is, 69.2% proved to be ALL. Significant p value was obtained in this relation.

On stain NSE out of 50 cases, 100% of them showed NSE negativity.

Splenomegaly was seen predominately in cases of AML accounting up to 70.6%, that is, a total of 12 AML cases and 5 cases of ALL showed splenomegaly.

Table 16: Clinical feature splenomegaly

Splenomegaly	ALL, *n* (%)	AML, *n* (%)	Total	χ^2	*P*-value
Not present	13 (39.4)	20 (60.6)	33	0.551	0.759
Present	5 (29.4)	12 (70.6)	17		

ALL: Acute lymphoid leukemia, AML: Acute myeloid leukemia

Table 17: Clinical feature hepatomegaly

Hepatomegaly	ALL, *n* (%)	AML, *n* (%)	Total	χ^2	*P*-value
Not present	14 (35.0)	26 (65.0)	40	0.087	0.768
Present	4 (40.0)	6 (60.0)	10		

ALL: Acute lymphoid leukemia, AML: Acute myeloid leukemia

Table 18: Clinical feature lymphadenopathy

Lymph-adenopathy	ALL, *n* (%)	AML, *n* (%)	Total	χ^2	*P*-value
Not present	14 (35.0)	26 (65.0)	40	0.087	0.768
Present	4 (40.0)	6 (60.0)	10		

ALL: Acute lymphoid leukemia, AML: Acute myeloid leukemia

Table 19: Cytochemical stains senstivity and specificity

Results Statistic	PAS		MPO		SBB	
	Value (%)	95% CI (%)	Value (%)	95% CI (%)	Value (%)	95% CI (%)
Sensitivity	88.89	65.29–98.62	93.75	79.19–99.23	75.00	
Specificity	96.88	83.78–99.92	100.00	81.47–100.00	100.00	81.47–100.00
Positive predictive value	94.12	69.77–99.11	100.00		100.00	
Negative predictive value	93.94	80.73–98.29	90.00	70.17–97.18	69.23	55.25–80.39
Accuracy	94.00	83.45–98.75	96.00	86.29–99.51	84.00	70.89–92.83

PAS: Periodic acid Schiff, SBB: Sudan black B, MPO: Myeloperoxidase

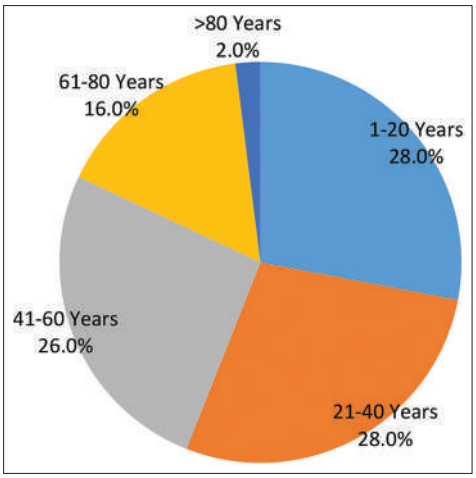

Figure 1: Age distribution of patients

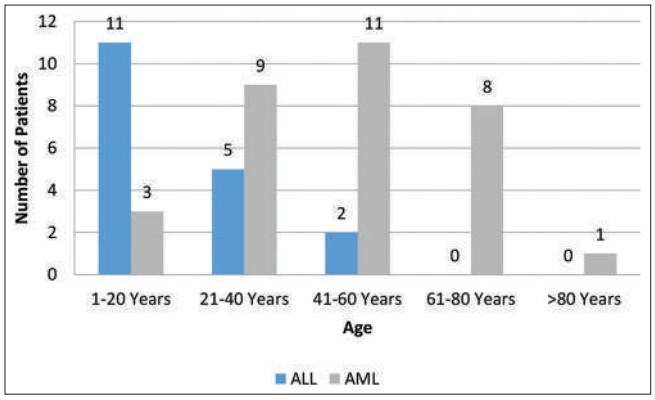

Figure 2: Age distribution of leukemia cases

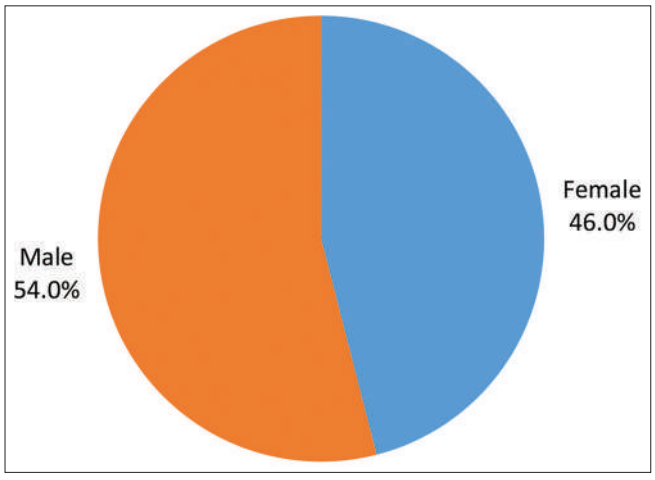

Figure 3: Sex distribution of cases

Hepatomegaly was seen in a total of 10 cases out of the 50 cases, constituting 60% of the AML cases.

Lymphadenopathy was seen in a total of 10 cases out of the 50 cases, constituting 60% of the AML cases.

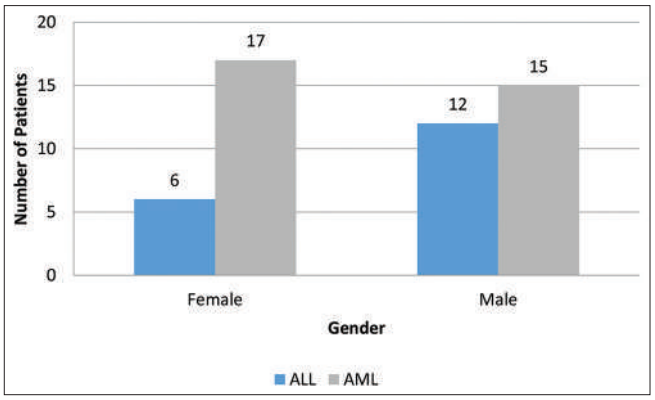

Figure 4: Sex distribution in cases of AML and all

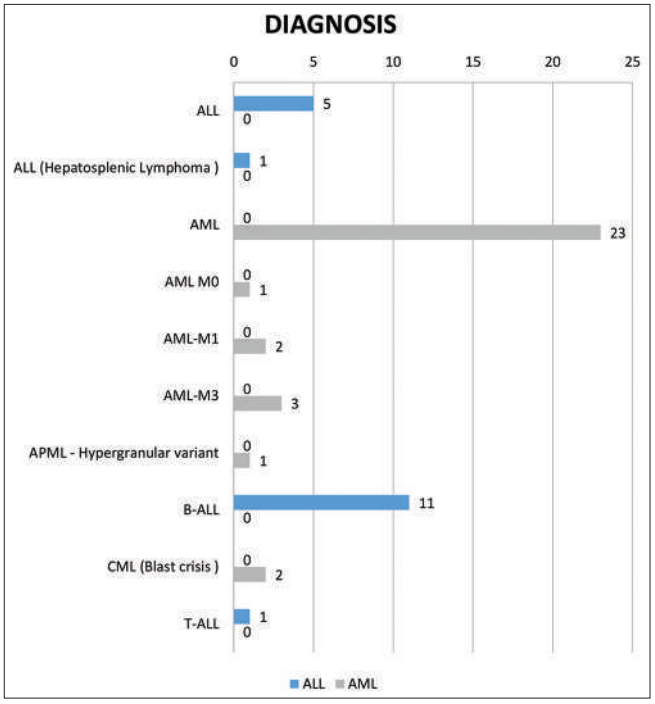

Figure 5: Distribution of patients according to types and sub types of leukemia

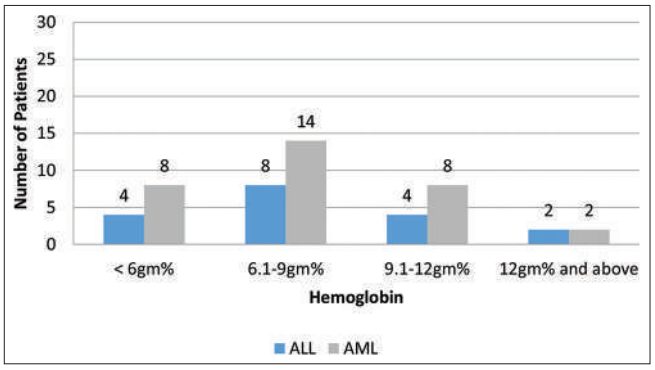

Figure 6: Hemoglobin distribution among the cases

As per our current study, the PAS stain shows sensitivity and specificity of 88.89% and 96.88%, respectively, in cases of ALL.

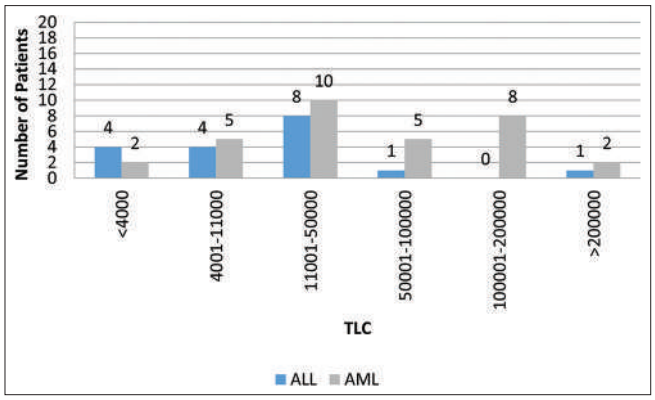

Figure 7: Total leukocyte count in cases

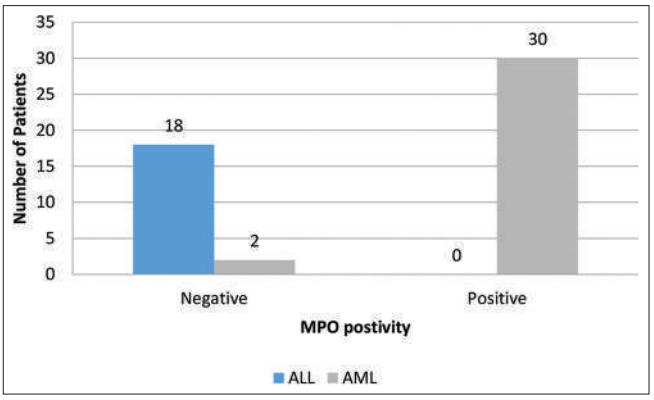

Figure 10: Cytochemical Stain-MPO

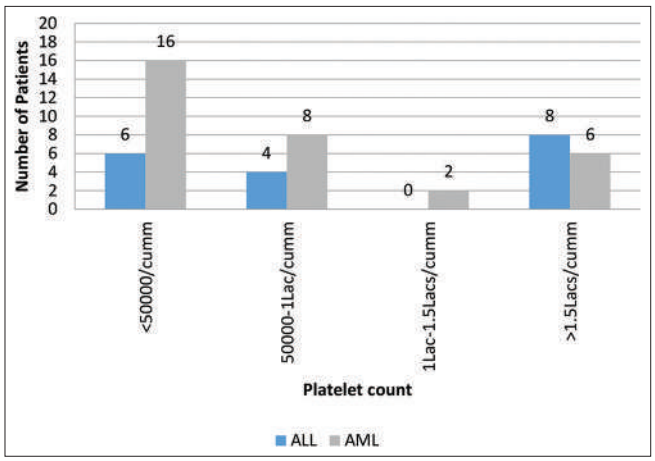

Figure 8: Platelet count in cases

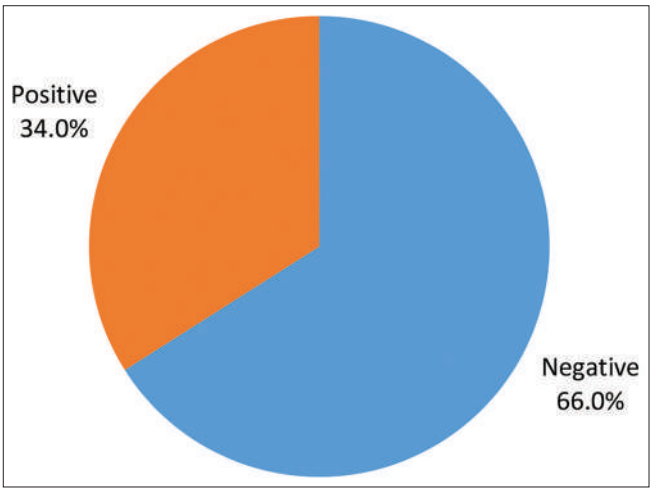

Figure 11: Cytochemical stain-PAS

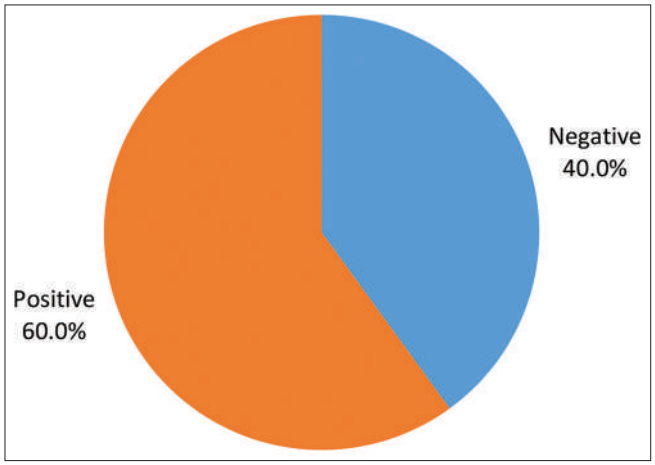

Figure 9: Cytochemical stain – MPO

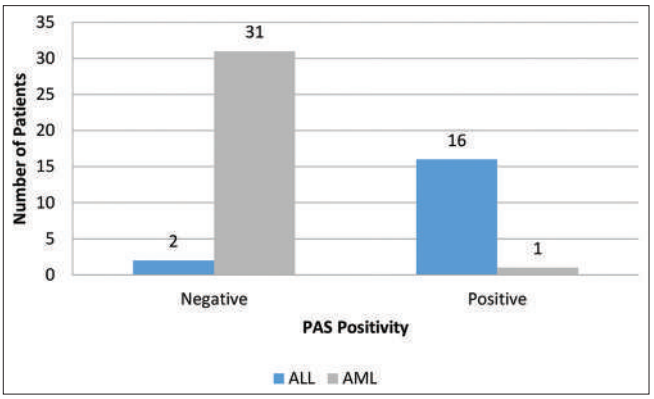

Figure 12: Cytochemical stain-PAS

The MPO stain shows a sensitivity and specificity of 93.75% and 100%, respectively, in cases of AML.

The SBB stain shows a sensitivity and specificity of 75% and 100%, respectively, in cases of AML [Figures 1-24 and Tables 3-19].

DISCUSSION

Age

In our study, the observed cases were in the range of 1–85 years. The majority of the percentage lying in the age group 1–20 years and 21–40 years, comprising 14 cases in each category, which was found to be 28% each, hence totaling to

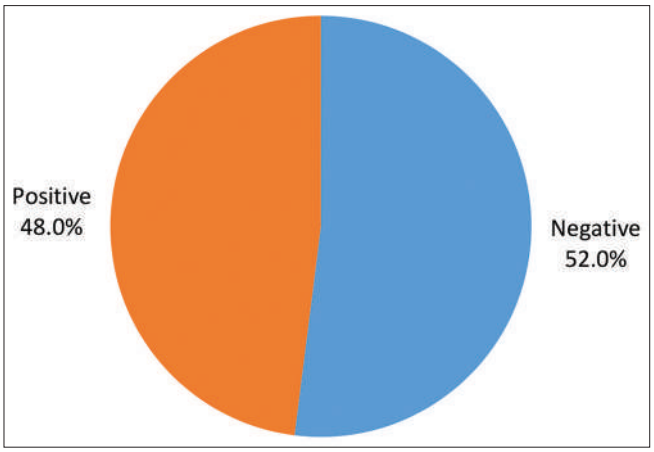

Figure 13: Cytochemical Stain – Sudan black B

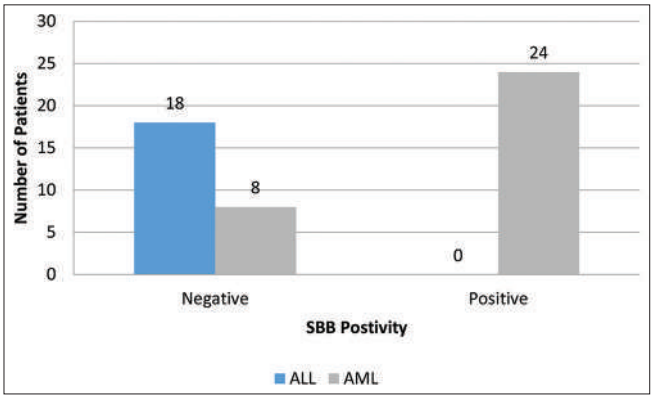

Figure 14: Cytochemical Stain-SBB

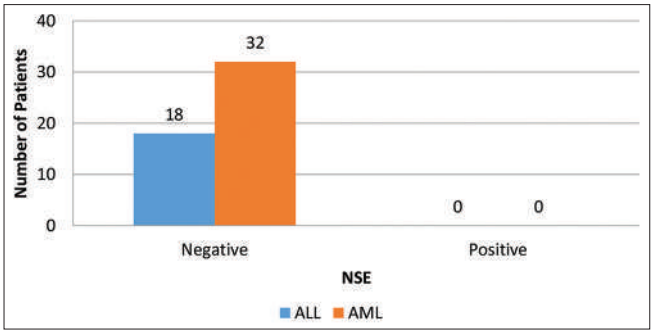

Figure 15: Cytochemical stain-non specific esterase

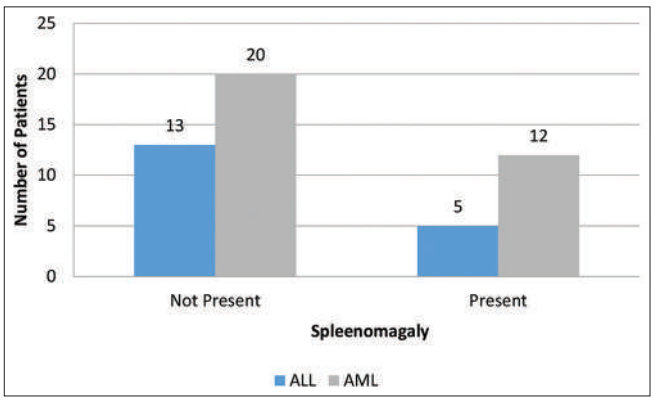

Figure 16: Clinical feature - splenomegaly

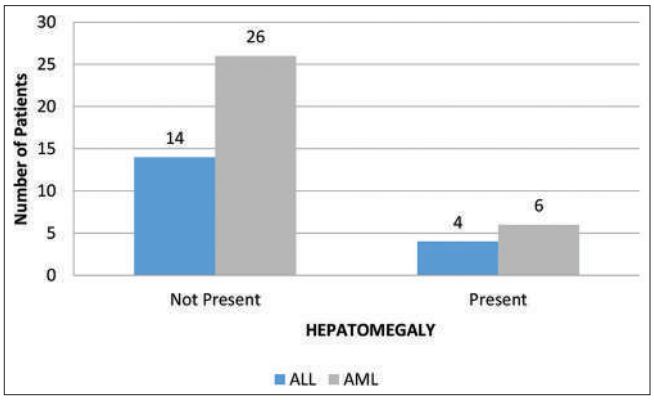

Figure 17: Clinical feature - hepatomegaly

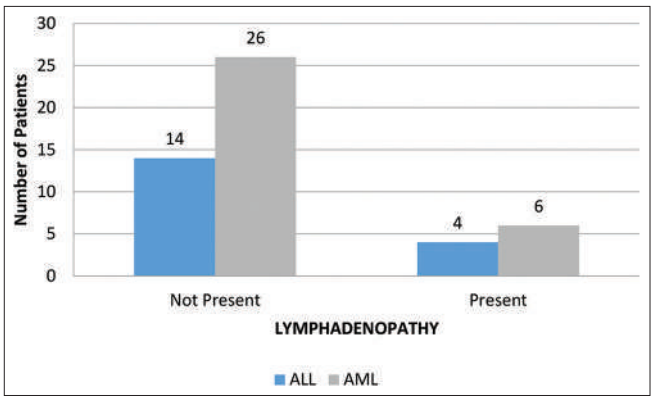

Figure 18: Clinical feature - lymphadenopathy

56%. Out of 14 cases in the category 1–20 years, 11 cases (78.6%) were of ALL and 3 cases (21.4%) were of AML. Whereas out of 14 cases in the category of 21–40 years of age, 9 cases (64.3%) were of AML and 5 cases (35.7%) were of ALL. This was followed by the age group 41–60 years, with 13 cases (26%), and 61–80 years group with 8 cases (16%), followed by the more than 80 years group with only 1 case, amounting to 2%. Therefore it was noticed that majority of ALL cases, that is, 11 out of 18 cases (61.1%) were found to be in the younger age group (1–20 years) and majority of AML cases, that is, 11 out of 32 cases were mostly seen in the middle age group (41–60 years).

Tegegen *et al*. in his study conducted on 40 cases of acute leukemia stated that 10 cases (25%) were less than 18 years of age while 30 cases (75%) were 18 and above.[23]

In another study conducted by Pandey *et al*. on 103 cases of acute leukemia, he discovered that the age group between 41 and 50 years old had the highest number of cases, that is, 19 (18.45%) followed by the age group between 11 and 20 years old which had 18 cases (17.5%) and the age group between 71 and 80 years old had the lowest number of cases, that is, 03 (2.95%).[24]

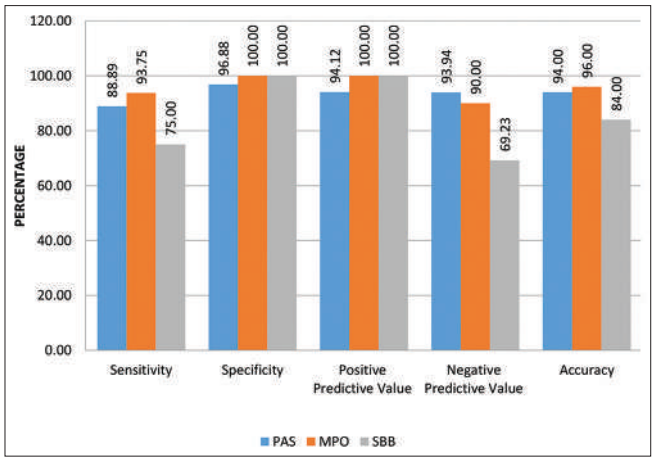

Figure 19: Cytochemical stains-sensitivity and specificity

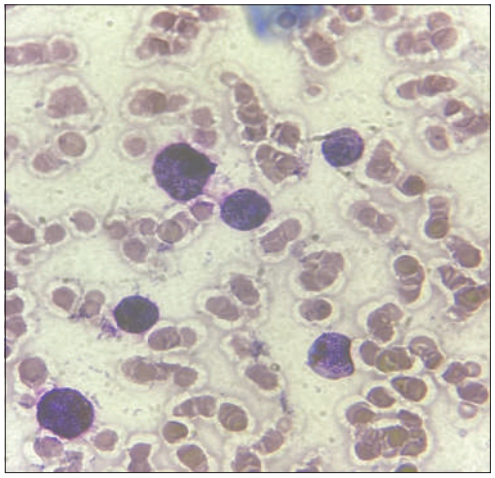

Figure 20: Microphotograph showing AML-SBB positivity

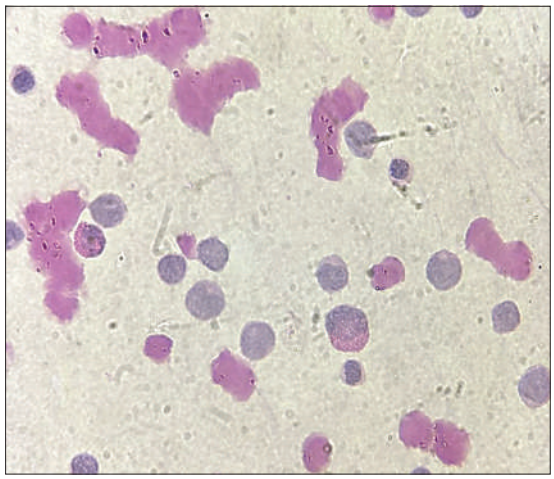

Figure 21: Microphotograph showing ALL-PAS positivity

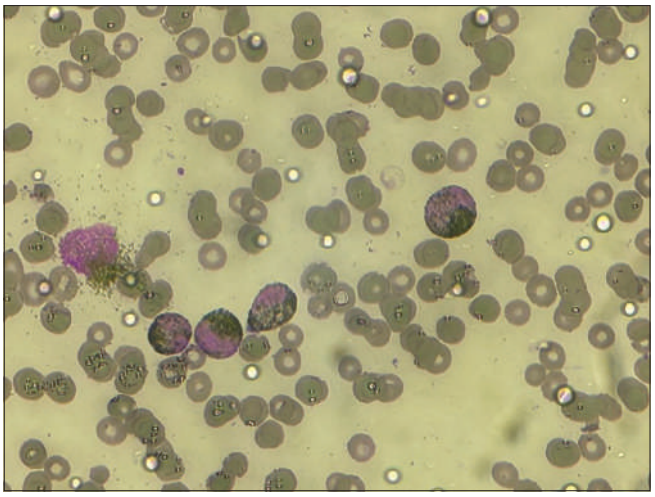

Figure 22: Microphotograph showing AML-MPO positivity

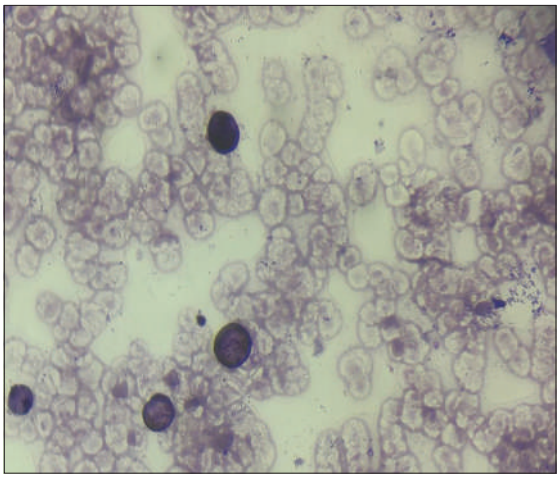

Figure 23: Microphotograph showing AML-SBB positivity

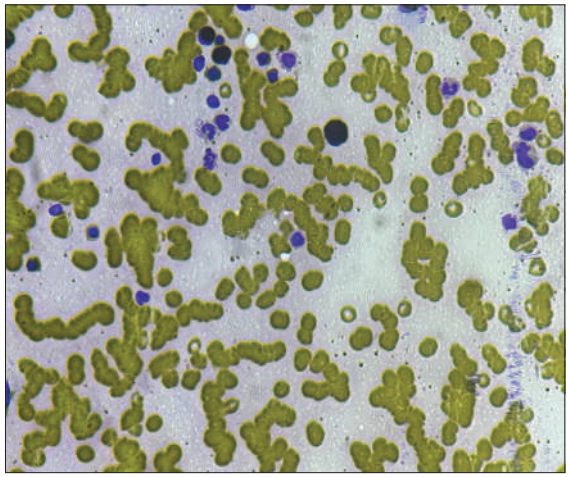

Figure 24: Microphotograph showing AML-MPO positivity

This was similar with the findings in the study conducted by Ratnamala *et al.* on 100 patients of acute leukemia, where he found that the age group of 41–50 years had the highest number of cases recorded, that is, 21 (21%), and the minimum number of patients were in the age group of 51–60 years having 12 cases (12%).[25]

Gender

In our study, out of the total 50 cases 27 were males (54.0%) and 23 were females (46.0%), so there was an almost identical sex distribution in our study. In another study conducted by Sahu *et al*. on 71 cases of Acute Leukemia, 42 cases (59.2%) were males and 29 cases (40.8%) were females. The findings of this study was comparable with our study.[26]

In the study conducted by Meena *et al*. on 36 cases, 24 cases (66.7%) were males and 12 cases (33.3%) were females.[27] In the study conducted by Tegegen *et al*. on 103 cases, 65 cases were males (63.1%) and 38 cases were females (36.8%). Hence, there was a significant male preponderance which was in contrast to our study.[23]

In our study, out of the 23 female patients, 6 were diagnosed as ALL (26.1%) and 17 were diagnosed as AML (73.9%). On the other hand, out of 27 male patients, 12 (44.4%) were diagnosed as ALL and 15 cases (55.6%) were diagnosed as AML. Therefore, it was observed that females showed higher prevalence of AML and males showed an almost equal prevalence of ALL and AML.

According to study conducted by Ahirwar *et al*. on 34 cases of acute leukemia, 23 cases were of ALL which showed a male preponderance, that is, 15 out of the 23 cases (65.2%) were males and 8 out of 23 cases were females (34.78%). On the other hand 4 out of 11 cases of AML were males (36.3%) and 7 out of 11 cases were females (63.6%). Therefore, ALL occurs more frequently in males than in females (1.87:1), and that AML occurs more frequently in females (0.57:1).[28]

Types of Leukemia

In our study, AML was found among 32 out of 50 cases (64.0%) and ALL among 18 out of 50 cases (36.0%). Out of the 18 ALL cases, 11 were of B-ALL (61.1%), 1 (5.55%) was diagnosed as Hepatosplenic lymphoma and 1 was of T-ALL (5.55%).

Tegegen et al. stated that out of 40 cases, 21 cases (52.5%) were identified as AML, and remaining 19 cases (47.5%) were identified as ALL. There were 10 cases of ALL that were determined to have B lineage leukemia cells (B-ALL), which accounts for 52.6% of the total, and there were 9 cases of ALL that were characterized as T lineage cells, which accounts for 47.5% of the total (T-ALL).[23]

Another study in Ethiopia based on morphology analysis by Shamebo *et al*., on 180 patients which demonstrated 85 cases (46.3%) cases of AML and 95 cases (53.7%) of ALL among acute leukemia cases during a 10-year period beginning in 1982 and ending in 1992. The previous study was conducted in Ethiopia. However, both investigations relied on patients who were diagnosed in a tertiary care referral center; as a result, the results of both studies may only be regarded approximations of the actual incidence of these leukemias across the country.[29]

Salem *et al*. conducted a research on 164 patients, which showed that 113 cases (68.9%) were classified as AML and 51 cases (31.1%) were of ALL. Out of the 51 cases of ALL, 38 cases (74.5%) were of B-ALL and 13 cases (25.1%) were of T-ALL. Hence, on comparing these studies with our current study we can clearly state that AML is much more common than ALL and, B-ALL shows a predominance over T-ALL.[30]

Comparative morpho-cytochemistry and immunophenotyping by flow cytometry were used in the research that Sengar et al. conducted on 100 individuals with acute leukemia who had not received any treatment. According to the data, there were 29 patients (29%) diagnosed with AML, 47 patients (47%) diagnosed with B-acute lymphoblastic leukemia (ALL), 20 patients (20%) diagnosed with T-ALL, and 4 patients (4%) diagnosed with biphenotypic acute leukemia. Only in the cases of AML was it possible for morpho-cytochemistry to establish a definitive diagnosis without FCM. Hence, in this study, ALL was the predominant Acute Leukemia in contrast to our study.[31]

Hemoglobin

In our present study, hemoglobin was seen to be lower than 12 g% in 46 out of 50 cases (92%), of which AML category showed that 22 cases (68.75%) out of 32 have Hb <9 g% with the majority of them lying in the range of 6.1–9 g%. Similarly, the majority of ALL cases had their Hb <9 g% accounting up to 12 cases out of the 18 cases (66.6%).

The study of Meena *et al*. done on 36 patients of AML reported that the majority of the cases, that is, 34 out of 36 had anemia (94.4%).[27]

According to research done by Ahirwar *et al*. on 34 cases of acute leukemia, it was seen that 13 of 23 (56.52%) patients diagnosed with ALL and 8 of 11 (72.73%) patients diagnosed with AML had a hemoglobin level of <6 g% (severe anemia). Hence, the findings were similar to our study.[28]

Total Leukocyte Count

In our current study, total leukocyte count was seen higher in cases of AML as compared to ALL. The majority of cases 18 out of 50 were seen to have their TLC between 11,001 and 50,000, in which 10 out of 18 cases (55.6%) were diagnosed as AML and 8 out of 18 (44.4%) cases were those of ALL. Hyperleukocytosis was observed in 13 of the total 50 cases, out of which 8 of 13 cases of AML

had their TLC between 1 lakh to 2 lakh, 1 of the 13 cases of ALL and 2 of 13 cases of AML had their TLC more than 2 lakh.

Meena *et al*. reported that 26 of the total 36 cases (72.2%) had their TLC more than 50,000/cumm. It was seen that 12 out of 26 of these cases (46.1%) had their TLC between 50000 and 99000/cumm. Hyperleukocytosis was noted in 14 out of 26 cases (53.9%) and out of these 3 cases had their TLC over 2 lakh.[27]

According to the findings of Choudhury *et al*., based on 100 cases studied, 49 of the 100 cases (49%) of the patients had leukocytosis, 32 of the 100 (32%) had leukopenia, and 19 of the 100 (19%) presented with a normal total count.[25]

Ahirwar *et al*. in their study conducted on 34 cases, found that 9 of 23 ALL cases (39.1%) and 7 of the 11 AML cases (63.6%) had leukopenia. Three of the 34 total cases (8.8%) had hyperleukocytosis.[28]

Platelet Count

In our present study, platelet count was seen to be reduced in most of the cases 36 of the total 50 cases (72%). 26 out of 32 cases (81.25%) of AML and 10 out of 18 cases (55.5%) of ALL had their platelet count <1.5 lakh/cumm. Platelet count of <50000/cumm, was seen in 22 cases, of which 6 (27.3%) were those of AML and 16 (72.7%) were those of ALL.

The symptoms of thrombocytopenia are usually described as early signs of the illness. According to research done by Ahirwar *et al*. on 34 patients of acute leukemia, 16 of the 23 ALL (69.57%) and all of the 11 AML cases (100%) had their platelet count less than. The results of these studies were similar to our current study.[28]

Pandey *et al*. reported that the most prevalent laboratory result was anemia, followed by thrombocytopenia, with a median platelet count of 33,000/cu.mm. This study was conducted on 103 cases, out of which 95 cases (93%) had thrombocytopenia.[24]

MPO

In current research, out of all the suspected cases of acute leukemia, 30 of the total 50 cases (60%) cases were MPO positive. All the MPO positive cases, turned out to be of AML series, whereas, out of all the MPO negative cases, 18 out of 20 (90%) were later proven to be ALL and 2 cases (10%) proved to be AML. A significant *P* value was obtained in this relation.

Kim *et al*. in his study conducted on 140 cases of AML showed that 86 cases (62%) were MPO positive and 54 cases (38%) were MPO negative.[32]

According to the study conducted by Pavithra *et al*. on 100 cases, 44 proved to be of AML series on FCM, out of these 44 cases, a concordance rate of 94.8% was observed between FCM and MPO positivity. cMPO was virtually uniformly expressed among the markers that were evaluated in the AML cases, with CD13, CD33, and CD117 also being expressed in the majority of patients as was seen our study where out of the 32 cases of AML, 30 cases had these markers, thus having similar results.[33]

In addition, our findings are in agreement with those of Paredes-Aguilera *et al*., who came to the conclusion that cMPO was the most sensitive marker for AML when compared to CD13, CD14, and CD33.[34]

PAS

PAS positivity was observed in 17 out of 50 cases, accounting up to 34% of all the cases taken. Out of all the PAS positive cases, 94.1% were proven to be those of ALL, and 5.9% proved to be AML on flowcytometry. PAS negative cases comprised of predominantly AML cases, that is, 93.9% and 6.1% cases were proven to be those of ALL. Significant p value was obtained in this relation.

Sahu *et al*. observed that on employing PAS stain on 49 cases of acute leukemia, 11 cases (22.44%) were PAS positive and 38 cases (77.55%) were PAS negative. 6 of the 11 (54.5%) PAS positive cases were those of ALL and 33 of the 38 (86.8%) PAS negative cases were of AML series.[26]

Hamid *et al*. studied 53 cases of acute leukemia and reported that 31 cases (58.5%) were of ALL and 20 cases were of AML (27.7%).This study showed that out of 28 PAS positive cases, 25 (80.6%) proved to of ALL series and 3 cases (15%) were of AML series.[35]

Aparecida *et al*. observed that 67 patients of acute leukemia were tested for PAS stain and showed that 31 cases (100%) of ALL were positive and in 1 of the AML cases (32.2%). These patients had concurrent diffuse and granular standard positivity, and their morphology was indicative of the monocytic lineage.[36]

SBB

In the present investigation, all the cases which were SBB positive were proven to be AML whereas the SBB negative cases showed that 30.8% of them later proved to be AML whereas the rest, that is, 69.2% proved to be ALL. Significant p value was obtained in this relation.

Aparecida *et al*. observed that SBB positivity was found in 29 out of the total 35 patients (82.5%) which proved to be of AML series and the 6 out of 35 cases SBB negative

cases were of AML. However, in our current study, all the AML cases proved to be SBB positive.[36]

SBB is not specific for myeloid series, and it may be positive in ALL, as reported by Stass *et al*., which demonstrated SBB positivity in 2 of 350 patients (2%) proven to be of ALL series and Deghady *et al*., studied 30 patients, demonstrating SBB positivity in of 13 of 15 (86.7%) AML cases and 2 out of 15 ALL cases (13.3%).[37,38]

Non Specific Esterase

In our present study, all the cases which were studied, that is, 50 of the 50 cases showed NSE negativity. In the study conducted by Deghady *et al*. on 30 cases, it was noted that no significant association was obtained with immunophenotyping. NSE positivity was noted in 2 of 15 (13.3%) cases of ALL and 6 of the 15 (40%) cases of AML.[38]

Study done by Sharma *et al*. showed that NSE stain was positive in some patients of ALL cases. This causes confusion with the monoblasts. However, if diagnosed with ALL, these patients have shown to have poorer outcome in the study conducted.[39]

In another study conducted by Wrotnowski *et al*. on 14 cases of Acute Monocytic Leukemia (M5) when stained with NSE stain had 2 varieties of granular staining: (1) Diffuse staining of finely granular cytoplasm and (2) dense focal staining of cytoplasmic granules.[40]

Splenomegaly, Hepatomegaly

In our current study, splenomegaly was noted in 17 out of the 50 cases (34.0%). Of these 17 cases, 12 were of AML (70.6%) and 5 were of ALL (29.4%). Hepatomegaly was seen in a total of 10 cases out of the 50 cases (20%), 6 of the 10 cases (60%) were of AML cases and 4 cases (40%) were of ALL. Lymphadenopathy was seen in a total of 10 cases out of the 50 cases (20%), constituting 6 of the AML cases (60%) and 4 of the cases were of ALL (40%).

Pandey *et al*. conducted a study on 103 cases and reported that only a small percentage of the patients showed concomitant findings such as splenomegaly in 31 cases (30.10 %), hepatomegaly in 12 cases (11.65 %), and lymphadenopathy in 19 cases (18.44%). Thus the findings were similar to our study.[24]

CONCLUSION

Hematogones and regenerating blasts are the most prevalent differentials of neoplastic blasts. These two types of blasts may be separated from one another by flow cytometric immunophenotyping. In this particular research, AML was shown to be the most prevalent form of acute leukemia. Furthermore, ALL was broken down into B-ALL and T-ALL subtypes. Flowcytometric immunophenotyping has a clear correlation with prognosis and, in an era where novel agents are being developed, may assist in the production of monoclonal antibodies that are specific to tumor antigens. Flow cytometry is the gold standard for evaluating minimal residual illness, particularly in instances when there is no clear molecular signature.

Morphology in conjunction with cytochemical staining continues to be the method of choice for the identification of acute leukemias, particularly in settings where immunophenotyping capabilities are unavailable, such as in the majority of medical centers located in developing and financially restraint nations like India. Although cytochemical stains are necessary for recognizing the subtypes of AML, they are of little help in identifying the subtypes of ALL. For this reason, the FCM has developed into a standard instrument for the assessment and management of patients who have leukemia.

Thus, considering our present study along with others stated, it must be noted that although cytochemistry and morphological analysis impacts the initial prognosis and therapeutic choices but the final diagnosis and mainstay of treatment is evaluated by the gold standard technique of flowcytometry.

Since comparative study was not in preview of my discussion, larger sample size in a Tertiary care Hospital is needed to carry out sensitivity and specificity of cytochemical stain versus flowcytometry in diagnosis of acute leukemia. Henceforth, in coming future, cytochemistry may become obsolete.

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Original Article

Ultrasound and Upper GI Endoscopy in Patients with Common Upper GI Complaints and its Risk Factors: A Observational Study

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Abstract

Introduction: Upper gastrointestinal symptoms are one of the most common complaints presenting to our outpatient services on a day-to-day basis. These range from simple epigastric pain to hematemesis, which are associated with many known risk factors such as smoking alcohol and others. However, these symptoms are same to some serious underlying pathology such as gastritis, gastroesophageal reflux disease, occult portal hypertension, and other gastric pathologies even gastric cancer; hence, a flexible upper gastrointestinal (GI) endoscopy with or without biopsy with helps us to evaluate these patients and detection of any serious pathology early and reduce the overall morbidity by early intervention if any necessary.

Materials and Methods: A study conducted at Siddhartha Medical College with 100 patients from convenient sampling with chronic upper GI symptoms and risk factors, it is an observational study.

Results: The sensitivity of ultrasound and endoscopy is comparable in setting of normal mucosa and gastritis, but endoscopy has better sensitivity in diagnosing gastric carcinoma and peptic ulcer disease as well as picking up varices in the lower esophagus and pathologies of duodenum.

Conclusion: Early endoscopic testing is required when patients have chronic upper GI symptoms and associated risk factors and with addition advantage of evaluating esophageal and duodenal pathologies.

Key words: GERD, LFT, NSAIDS, Ultrasound abdomen, Upper gastrointestinal endoscopy

INTRODUCTION

The phrase "upper gastrointestinal (GI) symptoms" is commonly used to describe a wide range of complaints including dyspeptic and gastroesophageal symptoms, as well as peptic ulcer disease.[1-4] Such symptoms are a common cause of healthcare utilization, resulting in increased direct medical costs[5] as well as costs to individuals and society due to lost work time and productivity (indirect costs), disrupted social life, and lowered quality of life (intangible costs).[5-7]

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GI symptoms such as heartburn, indigestion/dyspepsia, bloating, and constipation are common in the community. However, these symptoms may be misinterpreted and their impact and significance misunderstood both by health-care providers and patients.[8]

These are the common complaints affecting 25–40% of the general population during their lifetime.[9-11] In a systematic review, Heading[12] reported that prevalence of upper abdominal pain or discomfort ranged from 8 to 54%, while that of heart-burn ranged from 10 to 48%, for regurgitation from 9 to 45% and for both/either 21–59%. The prevalence of the upper GI symptoms varies with definition used, population involved (national vs. regional, Asian vs. Western), recall period, sex, and age.[13] Upper GI symptoms are a common cause of healthcare utilization and substantially affect the quality of life and psychological well-being of those affected.[7,14-16]

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Due to the recent increased interest in health and the National Cancer Screening Project, the demand for upper and lower GI endoscopy procedures is rapidly increasing. Although this applies to a training course in any field, mastering endoscopy basics is very important because when the process is imprecise or incorrectly performed, it can cause severe complications, endangering the patient's health or life.[17-19]

Insertion of the endoscope through the oral cavity and pharynx into the esophagus is the most difficult part of the process for trainee doctors. Incorrect technique can cause serious complications. Once the endoscope is inserted, detailed observation without blind spots is essential for a perfect procedure. Quality control in endoscopy procedures has recently come under heavy discussion; as such, the storage of endoscopy data, and photo images in particular, is very important. Specifically, when a patient is transferred for the treatment of a discovered lesion, photo images can be a very useful tool for exchanging opinions between doctors. Photo images are also useful in observing lesion changes during follow-up endoscopy, in educating trainee doctors, or in securing evidence in preparation for the remote possibility of a medical claim.[20-23]

Aim

The general aim of the study was to study the various endoscopic findings and its usefulness in patients with the upper GI tract (GIT) symptoms with or without alarm symptoms.

Objectives

The aims of this study were as follows:

1. To observe the causes and risk factor of the upper GIT symptoms
2. To observe the endoscopic presentation of the upper GIT symptoms
3. To observe the usefulness of endoscope and ultrasound (USG) in the diagnosis of the upper GIT symptoms.

MATERIALS AND METHODS

Study Setting

Study was done at Siddhartha Medical College and General Hospital, Vijayawada.

Study Design

It was a observational study conducted at Surgery Department of Siddhartha Medical College and General Hospital, Vijayawada.

Study Subject

Study has been included all clinically suspected patients with the upper GI symptoms and admitted in surgery department of Siddhartha Medical College and General Hospital, Vijayawada.

Inclusion Criteria

The following criteria were included in the study:

- Patients with age >18 years, showing symptoms of the upper GI for 4 or more than 4 weeks
- Patients with symptoms like
- Upper abdominal pain, vomiting's, hematemesis/melena, dysphagia, lump in abdomen, anorexia/weight loss, sensation of fullness after meals, weakness and tiredness, and retrosternal burning with regurgitation
- Patients with signs like
- Epigastric tenderness, supraclavicular lymph nodes, lump in the upper abdomen, visible upper abdominal peristalsis, and jaundice.

Exclusion Criteria

The following criteria were excluded from the study:

- Pregnant and lactating women, patients who are known cases of chronic pancreatitis and liver disease, and unwilling or unfit patients for endoscopy.

Sampling Technique

This study was convenient sampling.

Sampling Size

This study was 100.

Study Period

This study was November 2021–December 2022.

Data Collection Method

The data were collected from the patients using a semi-structured questionnaire. The sociodemographic factors will be taken by direct interview.

Investigations

The following investigations were routinely done before endoscopic examination:

- Screening for viral's, hemoglobin, stool for occult blood, LFT if jaundice is present.

RESULTS

Table 1: Age distribution of study participants (*n*=100)

Age (in years)	Number (%)
10–35	(19)
35–50	(40)
50–65	(29)
>65	(12)
Mean age±SD	50.3±6.4

Table 2: Gender distribution of study participants (*n*=100)

Gender	Number (%)
Male	(68)
Female	(32)

Table 3: Risk factor distribution of study participants (*n*=100)

Risk factor	Number (%)
Alcohol	(23)
Tobacco chewing	(18)
Smoking	(16)
NSAIDs	(4)
Aspirin	(2)
None	(37)

Table 4: Distribution of symptoms among study participants (*n*=100)

Symptoms	Number (%)
Blood in vomitus	9
Black colored stools	6
Abdominal distension	14
Epigastric pain	48
Dysphagia	16
Odynophagia	8
Change in voice	13
Retrosternal pain	35
Reflux	23

Table 5: Endoscopic finding among study participants (*n*=100)

Disease	Number (%)
Gastritis	(47)
Gastroesophageal reflux disease	(6)
Esophageal cancer	(2)
Esophagitis	(4)
Gastric ulcer	(10)
Gastric cancer	(2)
Esophageal varices	(5)
Duodenitis	(6)
Normal	(18)

Table 6: USG finding among study participants (*n*=100)

Disease	Number (%)
Gastric cancer	1
Portal HTN	4
Gastritis	47
Normal	48

Table 7: Sensitivity USG to predict upper gastrointestinal symptoms in study population (*n*=100)

Disease	Endoscopic findings	Detected right by USG	Sensitivity of USG (%)
Gastric cancer	2	1	50
Esophageal varices	5	4	80
Gastritis	47	47	100.0

CONCLUSION

The study titled an observational study "A observational study into findings of USG and upper GI endoscopy in patients with common upper GI complaints and its risk factors" was carried out in the period from November 2021 to December 2022 among 100 patients.

1. Highest number of participants (2/5th) belonged to age group of 35–50 years. Mean age was 50.3 years
2. Male: female ratio was 2.1:1. Male participants were almost double than female
3. Alcohol was the commonest risk factor observed among participants followed by tobacco chewing and smoking
4. Diabetes was the most common comorbidity observed among participants followed by fatty liver psychological stress. Almost 2/5th participants have more than equal to three comorbidities
5. Epigastric pain and retrosternal pain were commonest symptoms observed among participants
6. According to endoscopic finding, gastritis was found among almost half of the patients. Normal endoscopy
7. According to USG finding, gastric cancer was found among 1% of the patients. Normal USG was observed among 48 participants
8. Sensitivity of USG to diagnose to gastric cancer was very low but more than 80.0% sensitivity was found for USG in diagnosis of portal HTN.

SUMMARY

The present study was conducted with the aim to study the various endoscopic findings and its usefulness in patients with chronic upper GIT symptoms with or without alarming symptoms. In our observational study done among 100 clinically suspected patients with the upper GI symptoms and admitted in surgery department of Siddhartha Medical College and General Hospital, Vijayawada, during November 2021–December 2022, we found that endoscopy is far more relevant/reliable tool for diagnosing pathologies related to upper GIT with added advantage of finding esophageal pathologies and duodenal

pathologies. Since the symptoms and signs are less reliable indicators of the disease progression , and with added advantage of biopsy and intervention from endoscopy, it is always helpful to deliver the utmost and appropriate treatment to the patients suffering from chronic upper GI symptoms with risk factors.

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Original Article

Sarcopenia and Sarcopenic Obesity among Non-alcoholic Fatty Liver Disease Patients in North East India

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Abstract

Introduction: Non-alcoholic fatty liver disease (NAFLD) is an epidemic of new millennium. NAFLD and its complications are increasing with the prevalence of metabolic syndrome. Sarcopenia is considered to be complication of chronic liver disease. Chronic liver disease patients may be of a normal body mass index, or overweight or obese and yet be with sarcopenia. Sarcopenic obesity is defined as simultaneous presence of both sarcopenia and obesity.

Result: In this study, frequency and severity of sarcopenia and sarcopenic obesity in NAFLD was evaluated. NAFLD patients were categorized based on ultrasonography abdomen into grade 1, 2, and 3 and their skeletal muscle index was calculated after getting psoas muscle area by CT scan of abdomen. Out of total 110 patients, 17.3% patients were of grade 1 NAFLD, 39.1% patients were having grade 2 NAFLD, and 43.6% patients were having grade 3 NAFLD. In the correlation between sarcopenic obesity and NAFLD showed that 5.5% with grade 1 fatty liver, 25.5% with grade 2 fatty liver, and 43.6% of grade 3 NAFLD patients were having sarcopenic obesity.

Discussion: It was observed that sarcopenia and sarcopenic obesity is seen even in early stages of NAFLD. These patients can develop complications of chronic liver disease at an early stage.

Key words: Metabolic syndrome, Non-alcoholic fatty liver disease, Sarcopenia, Sarcopenic obesity

INTRODUCTION

Non-alcoholic fatty liver disease (NAFLD) is defined as presence of more than 5% fat in the liver (hepatic steatosis) either on imaging or on liver histology after exclusion of secondary causes of fat accumulation in the liver.

Sarcopenic obesity is defined as simultaneous presence of both sarcopenia and obesity. There is low muscle mass, instead of over-weight, or obesity as per body mass index (BMI). It is highly related with metabolism related disease, chronic disease, and functional disabilities and described as thin outside, fat inside.

Due to multisystem involvement, NAFLD is now renamed as metabolic (dysfunction) associated fatty liver disease.

NAFLD, non-alcoholic steatohepatitis (NASH), and sarcopenia share several features, such as chronic inflammation, oxidative stress, hormonal alterations, and decreased physical activity. Most of the cytokines found increased in patients with NAFLD and NASH are known to favor protein catabolism.

Reducing excess adiposity remains the fundamental pathogenic treatment for obese individuals, but it may however also compromise the ability to preserve muscle function and mass. Liver steatosis, cirrhosis, and liver cancer become a raising challenge for patients with long-standing obesity.

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In particular, in the pre-model for end-stage liver disease (MELD) score, when less strict criteria were adopted for patients, 8% increased risk of death per unit decrease in transverse psoas muscle thickness per height was observed. The ability of MELD score in predicting mortality was significantly increased when combined with muscle thickness measured [Table 1].

Earlier the causes of chronic liver disease and HCC were alcoholic hepatitis followed by viral hepatitis followed by NASH, but in recent years, the chronology has been changed and now the causes are, respectively, NASH followed by alcoholic hepatitis followed by viral hepatitis.

METHODOLOGY

In this study, 110 patients who were included who had minor gastrointestinal symptoms like dyspepsia was not having any clinical feature of chronic liver disease except mild to moderate hepatomegaly over a period of 2 years (2019–2021), after obtaining informed consent, sociodemographic data, personal history, and excluding significant alcohol history as per criteria Asia pacific association of study of liver. After enrolment vitals, waist circumference, fasting lipid profile, thyroid profile, LFT, FBS, PPBS, HBA1c, blood pressure, BMI, hepatitis B, and hepatitis C (for exclusion if positive) were studied. The study group patients were subjected to ultrasonography of abdomen to obtain the status and grading of NAFLD. Then, they underwent non-contrast computed tomography (NCCT) abdomen to see the cross-sectional area of psoas muscle at the level of L3 vertebra to calculate skeletal muscle index (SMI) as per designed and standard guideline.

Patients with viral hepatitis, alcohol intake history, and liver diseases of other known causes such as ATT, estrogen, or other drug-induced hepatitis were excluded from the study.

In NCCT abdomen scans, skeletal muscle tissue is separated according to different density thresholds. Density value of + 35 HU was used to separate fat from muscle tissue and + 150 HU to separate muscle from bone tissue. The L-3 SMI was expressed as cross-sectional mass area/m^2 [Figure 1].

- Non-contrast CT scans of abdomen, to measure the area of psoas muscle at the level of L3 vertebra is used
  - Skeletal muscle area: Males – 144.3 cm^2, Females – 92.2 cm^2
  - SMI: Males – 45.4cm^2/m^2, Females – 34.4 cm^2/m^2

L3 SMI = cross-sectional area of muscles at L 3 (cm^2)/ height^2 (m^2).

BMI was computed as body weight (kg)/height (m^2) was calculated by Quetelet index formula. In this study, Asia – Pacific BMI chart was used.

BMI with <18.5 considered underweight, 18.5–24.9 considered normal, 25–29.9 considered overweight, and >30 are considered as obese according to Asia – Pacific classification.

RESULTS

Male and female ratio was almost same. M: F: (48.2%: 51.8%).

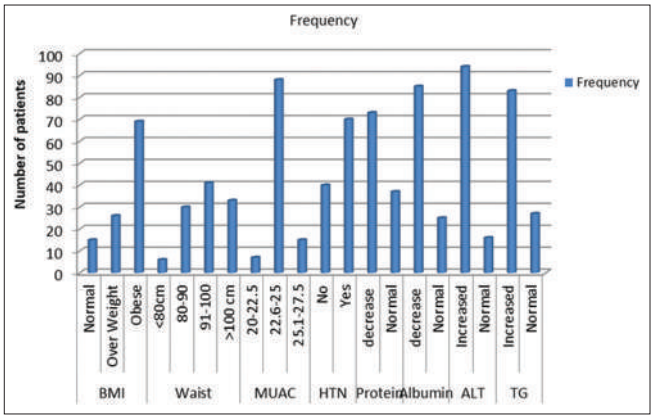

Figure 1: Bar diagram showing distribution of body mass index, waist circumference, hypertension, and triglyceride

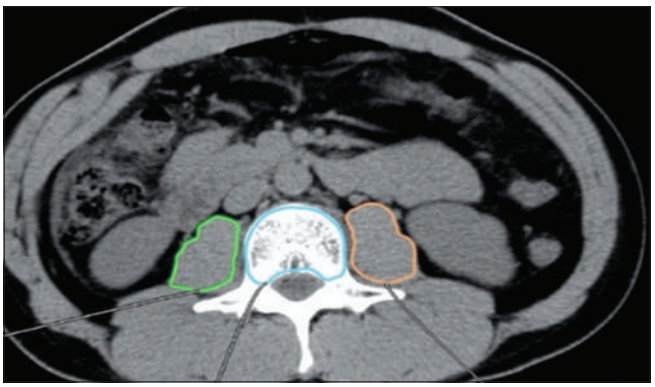

Figure 2: Non-contrast computed tomography abdomen showing psoas muscle cross-sectional area at the level of L3 vertebra

Table 1: Association between skeletal muscle index and USG abdomen

SMI	USG grade 1 (%)	USG grade 2 (%)	USG grade 3 (%)
15–20	0	0	13 (11.8)
21–25	0	0	27 (24.5)
26–30	0	16 (14.5)	8 (7.3)
31–35	2 (1.8)	10 (9.1)	0
36–40	6 (5.5)	11 (10)	0
41–45	0	4 (9.3)	0
46–50	11 (10)	2 (1.8)	0
Total	17.3	39.1	43.6

As per age group: (a) 16.4%: 21–30 years of age, (b) 24.5%: 31–40 years, (c) 34.5% 41–50 years, and (d) 24.5% 51–60 years of age. Comparatively more in 41–50 years of age group. In this study, 13.6% patients had normal BMI, 23.6% were overweight, and 62.7% patients were obese [Figure 2].

In the evaluation of association between sarcopenic obesity and NAFLD (diagnosed by USG abdomen) showed that 5.5% with grade 1 fatty liver, 25.5% with grade 2 fatty liver, and 43.6% of grade 3 NAFLD patients were having sarcopenic obesity.

It is important to know that normal Skeletal muscle index in males is 45.4 cm^2/m^2 and in females is 34.4 cm^2/m^2.

Out of 110 patients (n = 110), 62.7% were diabetic and 37.3% were non diabetic and 63.6% had hypertension (HTN). Triglyceride (TG) levels were increased in 83 (75.5%) patients, 67 (60.9%) of them had metabolic syndrome.

It was found that 57.3% of hypertensive patients, 54.5% of diabetic patients and 90.8% of patients with hypertriglyceridemia were having sarcopenic obesity.

DISCUSSION

The result of this study showed that maximum number of patients was having NAFLD and sarcopenic obesity in their late 40. Aging is accompanied by changes in body composition, like decrease in muscle mass, increase in abdominal adiposity, and ectopic fat deposition and insulin resistance.[1]

In the present study, 51.8% were female and 48.2% were male. The prevalence of NAFLD and sarcopenia tends to increase in post-menopausal women.[2]

In this study, 13.6% patients had normal BMI, 23.6 were overweight, and 62.7% patients were obese. Higher amounts of visceral relative to peripheral and subcutaneous adipose tissue are associated with greater risk of metabolic syndrome and are directly linked to liver inflammation and fibrosis, independent of insulin resistance, and hepatic steatosis.[3] In this group, normal weight individuals can be classified as metabolically obese normal weight and they demonstrate an increased risk for cardiometabolic risk.[4]

In the study group, 62.7% were diabetic and 37.3% were non diabetic, 63.6% had HTN. TG levels were increased in 75.5% and 60.9% of them had metabolic syndrome.

In this study, 57.3% of hypertensive patients, 54.5% of diabetic patients, and 90.8% of patients with hypertriglyceridemia were having sarcopenic obesity. Few studies showed that skeletal muscle is a major insulin responsive organ, loss of skeletal muscle, and myosteatosis can lead to a decrease in insulin response and energy expenditure, leading to increased hepatic gluconeogenesis, increased free fatty acid uptake and FFA oxidation.[5]

In recent studies, two different subtypes of NAFLD have been proposed based on lipid deposition. In subtype 1 based on insulin resistance, patients tend to have mono unsaturated TAGs and free fatty acids enriched with ceramides in liver. Subtype 2 based on carrying the PNPLA3 risk genotype have polyunsaturated TAGs.[6]

The prevalence of NAFLD was elevated among patients with T2DM, higher levels of waist circumference, BMI, TG.[7,8]

CONCLUSION

Sarcopenia begins to manifest in the early stages of NAFLD. Sarcopenia is preventable and disease modifying variable. The main intervention for preventing Sarcopenic obesity is physical activity which can cause certain weight loss and improve insulin sensitivity. But only physical activity can cause muscle mass loss if it is not supported with proper nutrition. Few studies have shown that Mediterranean diet, intermittent fasting can help with maintaining weight loss and insulin sensitivity. Adding resistance exercise to weight loss program can help prevent the reduction in muscle and bone mass.[9-11]

Screening for sarcopenia in early stages of NAFLD and treating it can improve the outcome as few studies have shown that higher skeletal muscle mass is associated with lower incidence of NAFLD and resolution of existing NAFLD.[12-14]

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Determining the Efficacy of Centchroman in Treatment of Mastalgia

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Abstract

Background: Breast pain or mastalgia is a common complaint among the woman presenting in surgical as well as gynecological OPD. Several non-medical and medical management has been tried for the treatment of mastalgia since ages. In this study, we have studied role of centchroman in treatment of mastalgia and also tried to observe its side effects and compliance.

Materials and Methods: It was a prospective observational study. Seventy-eight eligible patients fulfilling the eligibility criteria were enrolled for study. Each patient was given separate patient information sheet and proper counseling was done about the study and consent was taken. Tablet centchroman was give 30 mg bi weekly for 3 months. Follow-up was done at 1, 2, and 3 months and final closure was done at 6 months. The results were observed on a daily breast pain chart improvised by author.

Results: A daily breast pain chart was used in the study for assessment of pain. The minimum value was zero depicting no pain while maximum value was 4 indicating breast pain at rest. At the start of study, mean pain score was 1.44 ± 1.273. After 1 month, mean pain score became 0.764 ± 0.599, which is decrease of about 47%. By the end of 2 months, it was 0.548 ± 0.601 (decrease of 62%). It rose slightly to 0.690 ± 0.478 (approximately 20% rise in mean pain score than 2 months) level indicating that few patients were having recurrences. By the end of 6 months, mean pain score was 0.810 ± 0.647 indicating 43% decrease in mean pain score with respect to pain at beginning of the study. The side effects encountered in this study were mostly menstrual related which were temporary and normal menses were resumed on stopping medication.

Conclusion: This study shows that centchroman is a very effective drug for treatment of mastalgia with minimal and less severe side effects. It also shows less recurrence and patient is more compliant due to easy dosage.

Key words: Mastalgia, Cyclical, Non-cyclical, SERM, Centchroman

INTRODUCTION

Mastalgia comes from Greek word mastobreast and algia-pain. It was described in the medical literature as early as 1829. Mastalgia is a common complaint among women presenting in gynecology and surgical OPD.[1] Since most of the causes of mastalgia are of benign etiology, it needs symptomatic relief only. Mastalgia affects a woman's personal and sexual life along with constant fear of cancer, and hence, it needs to be given utmost importance while dealing with patient of mastalgia.

Mastalgia can be cyclical or non-cyclical based on its relationship with menstrual cycle. It can be intermittent or constant, localized, or diffused. Cyclical mastalgia is the most common type of breast pain accounting for two-third of cases.[2]

Mastalgia commonly occurs due to hormonal imbalance – estrogen excess, progesterone deficiency, changes in progesterone/estrogen ratio, differences in receptor sensitivity, disparate secretion of follicle-stimulating hormone (FSH) and luteinizing hormone (LH), low androgen levels, and high prolactin levels.

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Various drugs such as danazol, bromocriptine, tamoxifene, and LH-releasing hormone (LHRH) analogues have been used in the recent times for mastalgia, but most of them are known for their significant side effects.[3] In the search of a better remedy, there have been few attempts to try selective estrogen receptor (ER) modulator (SERM). Centchroman is one of such SERM synthesized by the Central Drug Research Institute, Lucknow, India. It was introduced as an oral contraceptive in the National Family Welfare Program India, in 1995. It antagonizes the effect of estrogen on uterine and breast tissue and agonizes its effects on vagina, bones, CVS, and CNS. It binds competitively to the ERs and antagonizes estrogen-induced gene expression.[4]

Centchroman had an advantage over the other steroidal oral contraceptives in not having side effects such as nausea, vomiting, weight gain, and dizziness. The other added benefit was its less frequent administration of twice weekly regimen. Due to its low dosage and less frequent administration, any effect over the hypothalamic-pituitary axis is minimal; hence, normal ovulatory cycles are resumed after withdrawal of the drug. It is safe in the treatment of unmarried women and those who wish to conceive after treatment. No teratogenic effect has been observed yet.

MATERIALS AND METHODS

This was a prospective observational study to compare the efficacy of centchroman in patients of mastalgia and also study its side effects and compliance. The study was conducted in Department of Surgery, ESIC Hospital, Varanasi, between December 2020 and July 2022. Patients in the age group of 16–40 years with cyclic or non-cyclic breast pain were included in the study. Patients were explained about the nature of study, drugs to be used, and its side effects. They were included in the study only after signing the consent from.

Exclusion Criteria

The following criteria were included in the study:

1. Age <16 years or more than 40 years
2. Benign breast lesions which require surgery for cosmesis
3. Women suspected or diagnosed with malignancy
4. Acute inflammatory breast lesions which are amenable to antibiotic or surgical drainage
5. Women who were planning pregnancy or pregnant women
6. Women with abnormal and undiagnosed uterine bleeding
7. Recent history of jaundice or hepatic impairment
8. Renal impairment
9. History of thrombosis.

Table 1: Comparison of age groups in various studies

Author	Types of study	Sample size	Age of patients	Outcome measures
Bansal *et al*.[5]	RCT	221	20–50	VAS
Dhar and Srivastava[6]	Clinical trial	60	17–35	VAS
Dhar *et al*.[7]	RCT	84	Reproductive age group	VAS
Karwasra *et al*.[8]	RCT	50	>18	VAS
Kumar and Hasan[9]	RCT	64	12–44	Breast pain chart
Mohakul *et al*.[10]	Prospective study	84	21–55	Pain scor e char
Shrivastava[11]	RCT	50	20–40	VAS
Tejwani *et al*.[12]	RCT	81	Reproductive age group	VAS+daily breast pain chart
Present study	Prospective study	78	16–40	Daily breast pain chart

Table 2: Comparison of types of mastalgia in various studies

Author	Total patient	Cyclical (%)	Non-cyclical (%)
Mohakul *et al*.[10]	84	37	63
Uma[13]	58	57	43
Present study	78	41	37

Detailed clinical history was taken to rule out acute conditions or history of malignancy in family. Routine baseline hematological and biochemical investigation was done in all patients. Initial clinical assessment and breast imaging was done with ultrasound (and mammography if age more than 35). FNAC of any lumps detected and cytological studies of the breast secretions if present were also done rule out malignancy.

Patients were provided with separate patient information sheet both in English and Hindi according to patient own language. The severity of Mastalgia was assessed using "The pain score" devised by author. It was different than standard visual analog scale (VAS) score commonly used.

The Pain Score

- Grade 4 – Breast pain at rest
- Grade 3 – Breast pain on movement
- Grade 2 – Pain on light palpation of breast
- Grade 1 – Pain on deep palpation of breast
- Grade 0 – No pain even on deep palpation of breast.

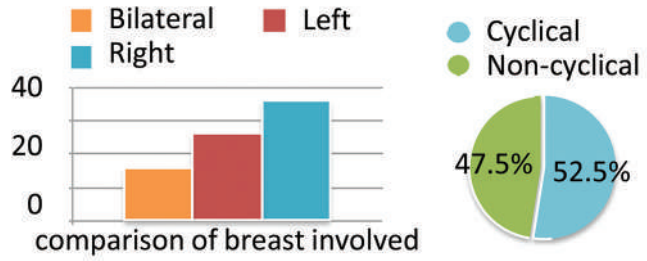
All the patients were taught and explained about grading of mastalgia. They were given a separate daily breast pain chart [Figure 1] and taught how to fill the chart and to bring it during each visit.

RESULTS AND ANALYSIS

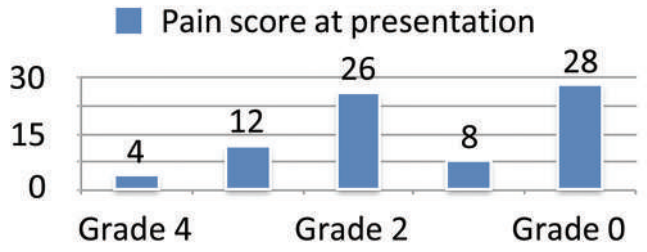
This prospective study was carried out in 78 cases of mastalgia who presented in surgery OPD of ESIC Hospital, Varanasi. The study was carried out between December 2020 and July 2022, and the data were collected in all these patients in terms of age, sex, clinical presentation, etiology, different severity score, ultrasound findings, side effects experienced, and compliance and follow-up was done after 1, 2, 3, and 6 months.

Age group	Number of patients	Percentage
≤20	24	30.8
21–25	24	30.8
26–30	14	17.9
31–35	6	7.7
36–40	10	12.8
Total	78	100

The study included 78 patients of mastalgia. Minimum age was 16 and maximum age was 40 with mean age of 24.97 ± 7.013 [Table 1]. Out of 78 patients, 62(79.5%) has disease in unilateral breast, whereas, 16(20.5%) has complaints in bilateral breast. Similarly out of 78 patients, 41(52.5%) had cyclical whereas, 37(47.5%) had non-cyclical mastalgia [Table 2].



Analysis of Pain Score [Table 3]



Comparison of Mean Pain Score

At presentation, 78 patients were enrolled. Mean pain score was 1.44 ± 1.273. After 1 month, mean pain score became 0.764 ± 0.599, which is decrease of about 47%. By the end of 2 months, mean score was 0.548 ± 0.601 (decrease of 62%). It rose slightly to 0.690 ± 0.478 (approximately 20% rise in mean pain score than 2 months) level indicating that few patients were having recurrences. By the end of 6 months, mean pain score was 0.810 ± 0.647 indicating 43% decrease in mean pain score with respect to pain at beginning of the study [Figure 2].

On detail follow-up, it was found that one patient loss to follow-up after 1 month and one patient after 3 months due to complete resolution of pain. One patient did not came for follow-up after 2 months due to some unknown reason.

Treatment of mastalgia

Various medical and non-medical methods have been adopted by doctors for treatment of mastalgia. In most patients with mild pain, reassurance is all that is required. A Brazilian study Barros *et al*.[14] verified overall success rate of 70.2% with reassurance in a study of 85 patients with mastalgia. The other non-medical means are dietary measures such as fat restriction and breast support with sport's brassier. The medical management includes use of drugs such as danazol, tamoxifen, bromocriptine, evening primrose oil, gamolenic acid (GLA), LHRH analogs, oral contraceptive pills (OCPs), and diuretics and topical NSAIDs gel. Centchroman is a non-steroidal, SERM drug formulated by the Central Drug Research Institute, Lucknow, India. In the present study, we studied effect of centchroman in mastalgia and we found out 43% decrease in mean pain score at the conclusion of study at 6 months.

In a study by Dhar and Srivastava using centchroman 30 mg on alternate day, drastic pain reduction was reported in 1 week period in 90% of the cases while almost all patients (n = 60) were painless at the end of 1 month.[6] Jain *et al*. reported a study of 60 cases where comparison was done between centchroman 30 mg daily versus tamoxifen 10 mg daily. More than 70% in both the group had complete pain relief by 3 months. There was no statistical difference in both groups.[15] In another randomized trial combining both alternate and daily dosage, Tejwani *et al*. reported centchroman to have response rate of 89.7% (reduction of pain to ≤3 on VAS) at the end of 12 weeks. Similar finding was found in study of Mohakul *et al*.[10] who reported 57% of patients to be pain free with the use of centchroman. Neogi *et al*.[16] concluded that pain relief was significantly better with centchroman after 24 weeks of treatment. Kumar and Hasan[9] reported similar reduction in symptom of mastalgia after 12 weeks of treatment. Karwasara *et al*.[8] concluded that patients showed gradual improvement in symptoms in terms of decrease in mean VAS during 3 months period of treatment (90%). This slightly higher percentage may be due dosage of centchroman. Centchroman was given on alternate day by Karwasara *et al*., while, in our study, we gave 30 mg biweekly. The similar result was seen in study by Kumar *et al*. who gave centchroman twice a week.

Table 3: Analysis of pain score

	Mean pain score at presentation	Mean pain score at 1 month	Mean pain score at 2 month	Mean pain score at 3 month	Mean pain score at 6 month
Minimum	0	0.0	0.0	0.0	0.0
Maximum	4	2.1	2.2	1.6	2.6
Mean	1.44	0.764	0.548	0.690	0.810
SD	1.273	0.5999	0.6014	0.4784	0.6472
Media n	2.00	0.700	0.400	0.500	0.800
Standard error of mean	0.204	0.1200	0.1254	0.1044	0.1412
z		−4.288[a]	−4.016[a]	−4.018[a]	−3.900[a]
Asymp. Sig. (two-tailed.)		0.00	0.00	0.000	0.00

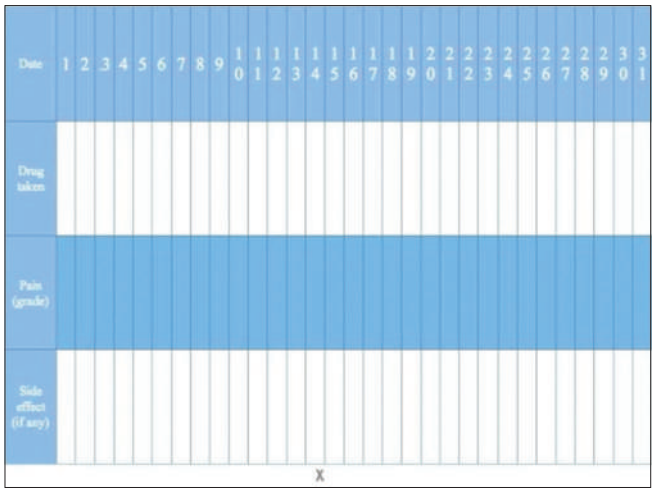


Figure 1: Daily breast pain self-recording chart

Analysis of Side Effects [Table 4]

On our first follow-up after 1 month, we found that out of 78 patients selected for study, one patient had loss to follow-up. Among the remaining 77, 71 (92.2%) had no side effects whereas 6 (7.8) experienced some kind of adverse effect. Two patients had oligomenorrhea, two had dizziness, and two patients had irregular cycle after taking the drugs. After 2 months, two patients (2.7%) had some kind of side effects while 75 (97.3%) had no effects. Of the two patients with side effects, one had complaints of oligomenorrhea, while other had delayed menses. Two patients loss to follow-up.

Similarly after 3 months, two patients had ovarian cyst on ultrasound scan. On last and final visit at 6 months (i.e., 3 months after discontinuation of drug), only one patient had ovarian cyst on ultrasound.

Analysis of Compliance

In this study, we tried to observe compliance of patient and found that the patient became more and more compliant due to efficacy, easy and less drug dosage, and less side effects.

Follow-up	After 1 month	After 2 months	After 3 months	After 6 months
Compliance (%)	89.5%	91.4%	97%	97%

DISCUSSION

Mastalgia was described in the medical literature as early as 1829 and it is derived from Greek word mastobreast and algia-pain. It is a common complaint amongst women of reproductive age group. Studies conducted on population-based and breast clinic-based[18] suggest that up to 70% of women under 55 years of age experience breast pain. Although 45% of them report minimal to mild symptoms, about 25% report moderate-to-severe mastalgia lasting for more than 5 days.

Classification

Mastalgia has been broadly classified into cyclical, non-cyclical, and extramammary musculoskeletal pain.[19]

A. Cyclical mastalgia: In cyclical mastalgia, discomfort commonly occurs around the menstrual cycle or ovulation, usually 2–3 days premenstrual. This is typically characterized by fine nodularity of breast before menstruation which subsides post-menstruation.
B. Non-cyclical mastalgia: Non-cyclical mastalgia lacks any relationship with the menstrual cycle. This falls

Table 4: Side effects of centchroman in different studies

Study	Oligomenorrhea	Delayedmenses	Irregular cycle	Dizziness	Urticaria	Ovarian cyst
Tejwani *et al*.[12]	31/41	6/41	2/4	0/41	0/41	0/41
Kumar *et al*.[17]	12/75	0/75	0/7	0/75	0/75	0/75
Kumar and Hasan[9]	24/64	2/64	1/6	0/64	0/64	0/64
Jain *et al*.[15]	2/30	2/30	0/3	8/30	0/30	5/30
Present study	3/78	3/78	2/7	2/78	0/39	1/78

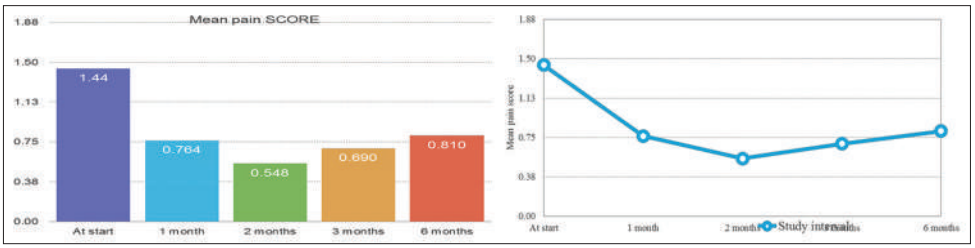


Figure 2: Variation of mean pain score

into two categories – true non-cyclical mastalgia and musculoskeletal pain. True non-cyclical mastalgia occurs in both premenopausal and postmenopausal women. This type of pain is well -localized to the breast especially in the sub-areolar and upper outer quadrants of the breast. Normally, the intensity and nodularity are less pronounced than that in the cyclical mastalgia.

C. Musculoskeletal pain is almost always unilateral (92%) and falls into two categories: Tietze's syndrome and lateral chest wall pain. In Tietze's syndrome, typically, the pain is felt within the medial quadrants of the breast and tenderness occurs on pressure over the affected costochondral junction.

Evaluation

The evaluation of mastalgia begins with a thorough history of pain, including the duration, site, severity, relationship with the menstrual cycle, and impact on everyday life. In non-cyclical mastalgia, the chest wall should be carefully palpated to exclude extramammary causes of the pain.

Etiology

Cyclical and non-cyclical mastalgia differ in the characteristics suggesting distinct etiology between these two forms.

Cyclical mastalgia is most severe before menstruation; therefore, a hormonal imbalance is suspected. Various theories were put to describe etiology of cyclical mastalgia. One of the earliest being edema due to water retention but Preece *et al*.[20] Later, the three hormonal theories were regarded as the etiology of mastalgia.

a. Increased estrogen secretion from the ovary
b. Deficient progesterone production (relative hyperestrogenism) and
c. Hyperprolactinemia.

The first two theories did not stand as earlier studies showed that there was no difference in the hormonal levels between the patients and the controls. A small but statistically significant difference in the prolactin levels between women with cyclical mastalgia and controls was recorded in a study, in which daily sampling of prolactin at a fixed time throughout the menstrual cycle was done. In a study by Peters *et al*., who examined, the stimulated prolactin response to thyrotropin-releasing hormone found that those with mastalgia had a significantly greater rise in prolactin compared to controls. However, the difference in the basal prolactin levels was not statistically significant between the groups, thus, strongly suggesting a disturbance of hypothalamic control in women with cyclical mastalgia.[21]

A definite role of ER in the pathogenesis of benign breast diseases is suspected based on a study done to estimate the value of ER. It was found that the patients with ER-positive breast disease responded better to danazol than patients with ER-negative breast disease.[22]

Possible causes of non-cyclical mastalgia include stretching of cooper's ligaments, pressure from brassiere, fat necrosis from trauma, focal/periductal mastitis, and Mondor's disease (sclerosing periphlebitis of breast veins).

Treatment of Mastalgia

Mastalgia affects both physical and mental health of patient. Apart from pain and discomfort, they are in constant fear of cancer. Therefore, the first step in treating women with mastalgia is to exclude malignancy and to counsel the patient.

Various methods have been tried for treatment of mastalgia which includes both medical and non-medical forms.

Non-medical Managements

1. Education and reassurance: The most successful treatment is the reassurance that a patient's symptom is not due to cancer. A Brazilian study verified on overall success rate of 70.2% with reassurance in a study of 85 patients with mastalgia. Reassurance was effective in 85.7% of the patient with mild form of mastalgia, in 70.8% with a moderate form, and in 52.3% with severe from
2. Well-fitting brassiere: Mastalgia may be due to active breast movement on the weak suspensory ligaments. Good external support by a sports bra can relieve most of the symptoms
3. Dietary measures: A number of dietary measures and therapies have been tried but on subsequent randomized trials have failed to demonstrate a clear advantage.

Medical Management

The drugs available for the treatment of mastalgia is topical NSAIDS, OCPs, diuretics, vitamin E, GLA, bromocriptine, tamoxifen, LHRH analogue, danazol, and the latest of them all being centchroman. All these agents have been tried with varying efficacy and side effects. There is no consensus about drug of choice for management of mastalgia.

- Topical NSAIDS: Topical application of NSAIDs was effective in mild type of mastalgia according to one study conducted in 2003, where diclofenac-diethyl-ammonium 2% gel was used.
- Oral contraceptives: OCP has been shown to have protective effect in benign breast diseases.
- Diuretics: There is no rational basis for the use of diuretics in the treatment of breast pain, which was demonstrated by the lack of correlation between retention of body water and symptoms.
- Vitamin E: Three RCTs had been conducted, all of which showed that vitamin E was no better than placebo in the treatment of benign breast disease.[23-25]
- GLA
- Evening primrose oil (EPO) had been introduced into the management of mastalgia based on the fatty acid deficiency hypothesis. It is rich in 7% linoleic and 72% linoleic acid which represent the richest natural source of essential fatty acids. Many trials have showed beneficial effects in mild and moderate mastalgia.[26] GLA is an essential polyunsaturated fatty acid (PUFA) present in large quantities in EPO. Low levels of the metabolites of GLA were found in women with cyclical mastalgia. As PUFA is denatured in the body by oxidation, adding antioxidants to PUFA were thought to enhance clinical response of PUFA. A Cardiff University study in 2005, on patients with mastalgia treated with GLA and placebo concluded that GLA efficacy did not differ from placebo, regardless of whether antioxidant vitamins were present.
- Bromocriptine: According to two different studies, significant reduction of cyclical mastalgia has been observed with bromocriptine 5 mg daily when compared to placebo.[27] It blocks the release of prolactin from the pituitary gland by dopaminergic receptor stimulation. In most women severe side effects have been noted, the commonest being nausea, vomiting, dizziness, headache, and postural hypotension. This could be overcome by increasing the drug doses gradually, and avoiding higher doses.
- Tamoxifen: A daily dosage of tamoxifen 10 mg has proven beneficial in both cyclical and non-cyclical mastalgia, with 98% and 56% response rates, respectively, according to a double blind study.[28] Side effects of short-term treatment characteristically include hot flashes, menstrual disturbances, weight gain, nausea, vaginal dryness, and bloating. A few rare yet serious side effects such as thromboembolic events, endometrial cancer, and cataracts have been reported in the literature; but their incidence in short-term, low-dose treatment regimens for mastalgia, is unknown.
- LHRH analog: In a randomized multicenter study on 147 premenstrual women with mastalgia treated with goserelin (LHRH analog) injection 3.6 mg/month for 6 months showed better outcome when compared to the placebo. Side effects include vaginal dryness, hot flushes, decreased libido, oily skin or hair, and a decrease in breast size which was more frequent than patients treated with placebo, thus making it the last resort in most of the refractory cases.[29]
- Danazol: Greenblat and co-workers introduced Danazol in 1971. Danazol is a synthetic testosterone which binds to progesterone and androgen receptors, but the precise mechanism of action in the treatment of mastalgia is unknown. It is a weak androgen, the isoxazole derivative of 17-a-ethinyl testosterone.

It acts at the hypothalamic level to prevent the rise in gonadotropins that would normally occur when estrogen and progesterone levels are low, without affecting basal gonadotropin concentrations. It interferes with FSH and luteinizing hormone at high doses. Thereby, it results in a low luteal progesterone level (suggesting anovulation) during treatment.[30] The usual dose of danazol in treatment of mastalgia is 100–400 mg per day. It has side effects such as amenorrhea and various androgenic effects such as weight gain, acne, and hirsutism. It is also a proven potential teratogen.

- Centchrom: Centchroman ($–C_{30}H_{35}NO_3$) is a novel non-steroidal, SERM, anticancer, and anti-osteoporotic drug, formulated by the Central Drug Research Institute, Lucknow, India. It was included in the National Family Welfare Program in 1995 as a "once a week pill." Since the early 1990s in India, centchroman has been available as birth control pill, and it is currently marketed there under the trade name Saheli. Centchroman binds competitively to the ERs and antagonises estrogen-induced gene expression. It shows weak estrogen agonistic and potent antagonistic activities but is devoid of progestational, androgenic, and antiandrogenic activities. Centchroman is free from side effects such as nausea, vomiting, weight gain, and dizziness. It does not delay return of fertility (after stopping) as it does not disturb ovulation and maintains normal ovulatory cycles. Centchroman has no apparent adverse effects on endocrine, hematologic, liver, and lipid function and has not been associated with any serious complications. After stopping this drug, there is an early return of fertility; therefore, it is safe in the treatment of unmarried women and those who wish to conceive after treatment. No teratogenic effect has been observed yet.

CONCLUSION

This study shows that both centchroman are very drug for treatment of mastalgia with minimal and less severe side effects. It also shows less recurrence and patient is more compliant due to easy dosage.

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Original Article

Evaluation of the Knowledge and Attitude of the School Teachers on Oral Health and Dental Trauma Management in Mathura City

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Abstract

introduction: Children spend a considerable amount of time in school, especially during their habit-forming time. Schools can provide an effective platform for promoting oral health in children. School teachers play an essential role in managing traumatic dental injuries.

Purpose: This study aimed to assess the knowledge and attitude of school teachers in Mathura city regarding oral health and first aid management of dental trauma.

Materials and Methods: In this cross-sectional study, 120 school teachers were selected through cluster sampling to answer the questionnaire. The data collected were sent for statistical analysis using the ANOVA test and *t*-test.

Results: The result of the study shows a fair knowledge of teachers on oral health and practices. However, knowledge of dental trauma management was inadequate among the school teachers of Mathura.

Conclusion: We conclude that although the school teachers had a fair knowledge of dental health and practices that there is still an immediate need for educational intervention to increase their knowledge and awareness regarding traumatic dental injuries and the protocol to be followed in school-going children.

Key words: Oral health, Knowledge dental trauma, School teachers

INTRODUCTION

Oral health surveys have concluded that the most common dental problems that occur are due to the lack of knowledge and awareness of dental health. It is very important to educate school children about oral health to instill a positive dental attitude at an early age for the development of good oral hygiene habits.[1]

Oral health means the health of the mouth and it is vital to general health and well-being.[2] Oral health not only causes tooth damage but is also responsible for a number of systemic infections. If left untreated they may affect the quality of life of the child, for example, the ability to eat and chew, the way they look and feel how they communicate. Pain from teeth or mouth compromises their focus and participation at school, thus preventing their proper development, and also forbidding full profit from schooling.

Teachers are role models for children to transmit good habits and values. The teachers should have a thorough knowledge and attitude toward oral health. They can play a major role in the early diagnosis and prevention of oral problems.[3] Traumatic dental injuries are a public dental health problem due to their frequency and occurrence at a young age. Statistics from many countries showed that one-third of preschool children suffered a traumatic dental injury of primary dentition while one-fourth of permanent dentition.

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Dental emergencies are also very common in school-going children, as they may injure themselves during playing, fights, etc. Complications after trauma include discoloration, coronal fractures, ankylosis root resorption, and avulsion.[4] Among the various types of dental injuries, avulsion leads to the greatest impairment of function and esthetics due to its poor prognosis. The primary and emergency management of such a situation is crucial to ensure a favorable treatment outcome.[5] Only a few children visit the dentist immediately as a result of dental trauma, which shows the lack of knowledge and awareness among the general population regarding the same.[6]

Hence, it is very important for the school authorities especially the teachers to have good knowledge about the protocols to be followed during these emergency situations. Therefore, this study aimed to assess the knowledge and attitude of school teachers on oral health and first aid management of dental trauma.

MATERIALS AND METHODS

A cross-sectional study was conducted among 120 school teachers in Mathura between January 2022 and May 2022. Data were collected in a questionnaire format. A structured self-administered questionnaire had been adopted and modified from the previous studies related to oral health and dental trauma in children.

Ethical approval for conducting the study was obtained from the Institutional Ethical Committee of the college and respective schools.

A questionnaire was prepared consisting of the following sections:

1. Knowledge and awareness about oral health problems and their prevention
2. Knowledge and awareness about the type and importance of the different types of dentitions
3. Knowledge about teachers' role in maintaining oral health among children.
4. Types of dental emergencies in school children and the related protocols to be followed.

Scores were given to each question. The maximum score was given to the correct answers and the minimum was given to incorrect answers. The scoring criteria were as follows:

- 75% and above – Good
- 50–75% – Average
- Below 50% – Poor.

With the permission of the principal of the respective schools, the questionnaire was distributed to the teachers. They were then collected back after 30 min which was followed by a PowerPoint presentation to educate the teachers about oral health and first aid management for dental trauma in children.

The data from the questionnaire were then tabulated and sent for statistical analysis. The statistical analysis was done using SPSS Version (20.0)

RESULTS

The results were tabulated, and conclusions were drawn.

Table 1 describes knowledge and awareness about oral health problems and their prevention. Most of the teachers were aware of oral health problems and their prevention. Around 63% of teachers concluded that "not brushing properly" causes tooth decay, while 25% of them concluded that "eating sweets and ice cream" causes tooth decay. About 7% suggested "not rinsing in-between meals" to be the reason for tooth decay, while only 5% of teachers thought "not regularly visiting a dentist" can cause tooth decay.

About 54% of teachers selected regular brushing and avoiding sweets and sticky foods as a way of preventing tooth decay while 20% thought regular brushing alone can prevent tooth decay. About 13% concluded that regularly visiting the dentist can prevent tooth decay while the rest 13% reported that rinsing in between meals can prevent tooth decay.

About 67% of the teachers were aware of the brushing techniques for children while the rest 33% were unaware of the techniques used for children. About 82% of teachers brushed twice daily, and 18% brushed once a day. About 45% of teachers changed their brushes every 3 months, while 55% changed their brushes every 6 months. All the teachers (100%) knew that it is important to visit a dentist periodically to maintain oral health. About 77% of teachers were aware that oral health can affect general health while the rest 23% were unaware of the fact.

When knowledge and awareness about the type and importance of the different types of dentitions were measured [Table 2], 65% of teachers were aware of the type of dentitions present in an individual at different ages of life. About 77% agreed with the fact that milk teeth are required for eating, speaking, and space maintenance while 23% did not agree with this fact.

When knowledge about teachers' role in maintaining oral health among children was measured [Table 3], 80% knew

Table 1: Knowledge and awareness about oral health problems and their prevention

1. A/c to you what are the causes of tooth decay	Eating sweets and ice cream: 30=25%	Not brushing properly: 76=63%	Not rinsing in-between meals: 8=7%	Not regularly visiting a dentist: 6=5%
2. Prevention of tooth decay can be done by?	Regular brushing: 24=20%	Regular brushing+avoiding sweets and sticking foods: 64=54%	Regular dental visit: 16=13%	Regular rinsing between meals: 16=13%
3. How to prevent gum bleeding?	Regular brushing: 8=7%	Flossing: 6=5%	Mouthwash: 14=12%	All of the above: 92=76%
4. What is the frequency of brushing?	Once-daily: 22=18%	Twice daily: 98=82%	Thrice daily: 0=0%	More than 3 times: 0=0%
5. How often do you change your brush?	Monthly: 0=0%	3 monthly: 54=45%	6 monthly: 66=55%	Yearly: 0=0%
6. Are you aware of the brushing techniques for children?	Yes: 80=67%	No: 40=33%		
7. Do you think it is important to visit a dentist periodically to maintain oral health?	Yes: 120=100%	No: 0=0%		
8. Did you notice any of your students missing their school because of dental pain?	Yes: 86=72%	No: 34=28%		
9. Have you ever seen a decayed tooth and how does it appear?	Yes: 76=63%	No: 44=37%		
10. If yes, do you check the children oral cavity periodically and make necessary referral?	Yes: 52=43%	No: 68=57%		
11. Do you think that oral health affect general health?	Yes: 92=77%	No: 0=0%	No idea: 28=23%	

Table 2: Knowledge and awareness about the type and importance of the different types of dentitions

1. What are the dention an individual has?	Primary dentition: 14=12%	Permanent dentition: 28=23%	Both: 78=65%
2. Do you agree milk teeth are required for eating, speaking and space maintenance?	Yes: 92=77%	No: 28=23%	

Table 3: Knowledge about teachers' role in maintaining oral health among children

1. Can teachers play effective role in oral health promotion?	Agree: 96=80%	Not sure: 24=20%	Disagree: 0=0%	
2. Does your teaching curriculum includes education regarding teeth and their importance to children?	Yes: 76=63%	No: 44=37%		
3. What kind of oral education have you given your school children?	About tooth types, functions, structure, eruption: 8=6%	About brushing, good dietary habits, injurious oral habits: 30=25%	Education about tooth decay, gum diseases, irregular teeth, their causes and prevention: 20=17%	All of the above: 62=52%
4. Till now any dental health camp was conducted in your school?	Yes: 62=52%	No: 58=48%		

that teachers play an effective role in oral health promotion while 20% were unsure. About 63% of teachers stated that their teaching curriculum includes education regarding teeth and their importance to children, while 37% reported that their curriculum did not include education regarding oral health and its importance.

When types of dental emergencies in school children and the related protocols to be followed were measured [Table 4], 68% of teachers reported that they have come across dental emergencies in the form of tooth/teeth loss in their school while the rest 32% reported that they have not come across any such dental emergencies. About 67% of teachers knew that the broken piece of a tooth is useful while 33% were unaware of the fact. About 70% of teachers knew the fact that after a complete loss of a permanent tooth, it can be replaced back while the rest 30% were unaware of this. About 58% of teachers did not know that a lost tooth can be stored either in coconut water, milk, or patient's own saliva and carried to the dentist immediately while the rest 42% were aware of this fact.

DISCUSSION

A child during his pre-primary and primary school time period goes through an active developmental stage and so during this stage, the teachers can greatly influence their health behavior.[3] Well-informed teachers have a great

Table 4: Types of dental emergencies in school children and the related protocols to be followed

1. Did you come across any dental emergency in the form of tooth/teeth loss in your school?	Yes: 82=68%	No: 38=32%
2. If a tooth is broken do you know that the broken piece is useful?	Yes: 80=67%	No: 40=33%
3. If complete loss of permanent tooth occurs: Do you know it can be re-implanted?	Yes: 84=70%	No: 36=30%
4. If yes do you know that it should be stored in either in coconut water, milk, patient's saliva and carried to the dentist immediately?	Yes: 50=42%	No: 70=58%
5. If given a chance will you be keen on receiving more information regarding dental injuries and its management	Yes: 115=96%	No: 5=4%

potential in providing good oral health education and thereby instilling a positive dental attitude in children at an early stage of life.[4] This could be achieved only if the teachers are aware of the oral health problems and their prevention.

This study was conducted with the aim to assess the knowledge and attitude of school teachers on oral health and dental trauma management in school children. According to the best of our knowledge, no such study has been conducted among school teachers in the Mathura district.

The overall knowledge of the school teachers on oral health was fair. In our study, 63% of subjects reported not brushing properly to be the cause of tooth decay which is similar to the study done by Maganur *et al.,*[3] in which 58% of the subjects concluded not brushing properly that is the main cause of dental problems.[3] A similar study was conducted by Shekhar *et al.* and only 14.2% of subjects concluded that tooth decay can be prevented by regular brushing and avoiding sweets, while, in our study, 54% concluded that regular brushing and avoiding sweets and sticking foods can prevent dental caries.[7]

In present, 82% of the teachers reported that they brushed their teeth twice daily, and 18% brushed once a day, this was similar to the study conducted by Mota *et al.*[8] The teachers showed fair knowledge and awareness of oral health problems and their prevention. About 77% of teachers were aware of the fact that oral health affects general health, while 23% of the teachers had no idea on this. In another study conducted by Maganur *et al.,* 100% of the teachers were aware of the fact that oral health affected general health.[3]

The majority of teachers (65%) in the study were aware of the type of dentition an individual has. Most of the teachers knew the importance of primary teeth for eating, talking, and space maintenance. About 80% of the teachers agreed to the fact that teachers can play an effective role in oral health promotion.

According to the results of the present study, 82% of teachers did not receive any training for dental emergencies. This finding was in accordance with Chandukutty *et al.*[9] About 70% of the teachers knew that if complete loss of permanent teeth occurs that it can be re-implanted, while 30% of the teachers were unaware of this fact. A similar study was conducted by Mohamed, in which it was observed that 41.2% of teachers were aware of the re-implantation of permanent teeth, while 58.8% of teachers were unaware of this[1] which indicates inadequate knowledge regarding traumatic dental injuries and the need for in-service dental emergency training for school teachers.

The time-lapse after avulsion and storage media is two of the most important factors for preserving the periodontal ligament cells and thereby improving the prognosis of an avulsed tooth. On being asked if they knew that a lost tooth should be stored in either coconut water, milk, or the patient's saliva and carried to the dentist immediately, 42% answered yes while 58% were unaware of this fact. Another similar study was conducted by Prasanna *et al.* according to which 88% of teachers were unaware of the storage of an avulsed tooth.[10]

School teachers' overall knowledge about dental emergencies among school children was not really up to the mark suggesting the need for educational interventions. This was similar to the study conducted by Yilmaz *et al.*[11] which stated that the teacher's knowledge about dental trauma management was inadequate.

The current results revealed that 96% of the teachers were keen to receive more information on dental injuries and their management, which is in agreement with the previous results in literature among the different population.[6,10,11] The majority of the teachers felt that educating children about oral health could prevent most dental diseases. School teachers in the present study demonstrated fair oral health knowledge, oral practices, and favorable approaches to children's oral health.

Overall results of our study showed a positive attitude toward managing traumatic dental injuries although their knowledge is inappropriate. The results revealed that the majority of the teachers neither received any first aid training nor any dental trauma management. Providing oral health education in schools not only develops personal skills but also instills a positive dental attitude and healthy behavior

among school children at an early and developing stage of life. Hence, first aid and trauma management training should be made compulsory for all primary school teachers.

CONCLUSION

The findings of our present study indicate that the school teachers in Mathura showed satisfactory oral health knowledge and their attitude toward oral health education. Their knowledge of dental trauma and its management was inadequate. There is an immediate need for educational intervention to increase their knowledge and awareness regarding traumatic dental injuries and the protocol to be followed in school-going children.

RECOMMENDATION

1. Dental emergency education program should be made a part of the annual health educational course carried by the school management.
2. Educational posters and pamphlets should be circulated in schools.
3. More school oral health programs should be conducted in schools.

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Original Article

Umbilical Artery Doppler to Determine the Relation between Doppler Indices and Sampling Site in the Third Trimester of Pregnancy: A Prospective Study

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Abstract

Background: The most useful tool for identifying and treating fetal growth restriction is the umbilical artery (UA) Doppler. The components of obstetric Doppler include the middle cerebral artery, UA, uterine artery, and ductus venosus. The optimal site to sample the UA is simultaneously one of the most frequently requested questions, so this study was done to determine the changes in umbilical pulsatility index (PI) and resistivity index (RI) at several sites.

Purpose: The purpose of this study was to ascertain whether the UA's RI and PI values differ at various sample sites during normal third-trimester pregnancy and whether its sampling next to the fetal bladder can be used for serial monitoring of fetal well-being.

Materials and Methods: A prospective observational study was conducted in Kempegowda institute of medical sciences with a study population of 312 third-trimester antenatal cases. All patients who met inclusion criteria underwent UA Doppler sampling at four different sites: At the placental attachment site, free-floating loops, abdominal attachment site, and beside the fetal urinary bladder.

Results: The mean RI and PI value of the UA was highest beside the fetal urinary bladder and lowest at the placental attachment site suggesting a significant difference.

Conclusion: Our findings of different Doppler indices based on the UA sampling site have important implications for the clinical surveillance of the fetus for subsequent care. The site of sample will be a crucial factor in assessing the severity of abnormality whenever UA Doppler indices are aberrant. Whenever we encounter any difficulty in locating a fixed place for monitoring, we can alternatively conduct the UA sampling next to the fetal urinary bladder.

Key words: Intra-uterine growth restriction, Middle cerebral artery, Pulsatility index, Resistivity index, Umbilical artery Doppler

INTRODUCTION

Ultrasound is the modality of choice in pregnancy. It has the most potential impact in managing high-risk pregnancies, including a high risk for fetal intrauterine growth restriction (IUGR) or where IUGR is already established.[1] Two umbilical arteries carry the deoxygenated blood from the fetus to the placenta.[1] The umbilical arteries arise from the fetal internal iliac arteries coursing alongside the lateral walls of the bladder into urachus[1] [Figure 1]. The umbilical artery (UA) measures 55–60 cm in length,[2] and its sampling plays a major role in assessing fetal growth restriction/distress. The Doppler parameters of UA mainly depend on the Doppler angle, sampling site, fetal cardiac, and breathing movements.

Normal waveforms from the UA are unidirectional and demonstrate forward flow throughout the cardiac cycle [Figure 2]. An abnormal waveform shows absent or reversed diastolic flow. Before the 15th week, the absence

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of diastolic flow may be a normal finding.[3] Depending on the fetal gestational age, any of these abnormal/aberrant findings should cause us to be concerned and take the appropriate therapeutic action. An increase in resistivity index (RI) and pulsatility index (PI) values is the early indicator, even when the wave patterns are normal.

Routine sampling of the UA is done at the free-floating loops, because many previous studies have shown to sample at these free loops. It is however challenging when continuous monitoring of intra-uterine growth-restricted fetuses by Doppler is required since the repeat values may be high if sampling is done toward the placental attachment site and less if we measured near the fetal attachment site of the umbilical cord. Therefore, in this study, we are trying to determine the difference in angle-independent indices of fetal Doppler at different sites of the UA and whether a fixed site (beside the fetal urinary bladder) for a sampling of UA can be determined for serial monitoring. Sampling of the UA beside the fetal urinary bladder is straight forward since this site is constant, and not only the number of umbilical arteries can be easily identified in the early pregnancy/NT scan but also effectively sampled in case of oligohydramnios, twin pregnancies, and other conditions where free loops' identification is difficult. Normally absent/reversed end-diastolic flow is likely to be seen first at the fetal end; thereby, we can find whether the Doppler values are statistically significant, which will help in early intervention and reduction of perinatal mortality.[4]

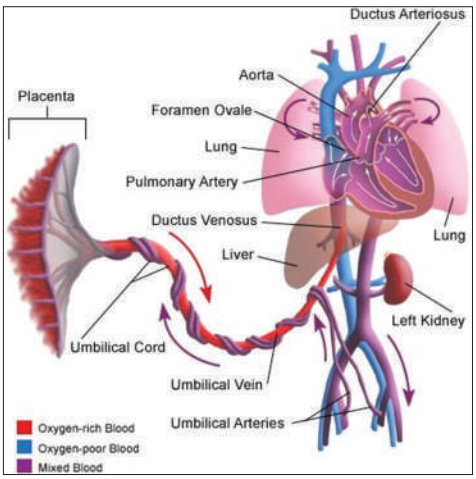

Figure 1: Anatomic image of fetal circulation in oblique view showing umbilical artery origin from internal iliac arteries and carrying deoxygenated blood to the placenta

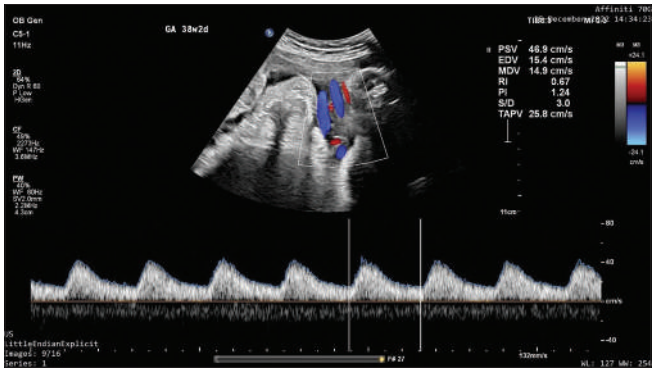

Figure 2: Normal wave pattern of umbilical artery: Duplex ultrasound image of a 38-week 2- day fetal umbilical cord sampled at free loop showing continuous unidirectional and forward flow throughout the cardiac cycle

Aims and Objectives

The aim of the study is to determine the difference in RI and PI values of the UA in different sampling sites along its length in a normal third-trimester of pregnancy.

The main objective is to determine a fixed location, like beside the fetal urinary bladder (Perivesical location) can be used for the UA sampling in serial monitoring.

MATERIALS AND METHODS

Study Design

This study was a prospective study.

Duration

This study was 1 month.

Place

This study was Kempegowda Institute of Medical Sciences (KIMS) hospital, Bangalore.

Sample Size

This study was 312.

Inclusion Criteria

The following criteria were included in the study:

- All normal third-trimester pregnancies.

Exclusion Criteria

The following criteria were excluded from the study:

- High-risk pregnancies
- Complicated pregnancies (GDM, HTN, and pregnancy associated with other maternal conditions)
- Pregnancy with IUGR.

This is a prospective study conducted in the Department of Radiodiagnosis KIMS, Bangalore, over a month in 2023. Normal pregnancies who came for routine antenatal scans and those who agreed to participate in this study were included in the study.

Prior Ethical Committee Clearance and patient consent were taken.

Using an affinity 70 ultrasound machine with all safety precautions and the ALARA principle, obstetric Doppler studies were conducted by a single radiologist with 12 years of experience in fetal ultrasound and obstetric Doppler sonography.

Doppler was performed with the mother in the supine position, and parameters were obtained when the fetus was not Mobile. Using a curvilinear probe (frequency 2–6 MHz) with appropriate Doppler settings, RI and PI values were obtained.

UA Doppler sampling was done at four sites: the placental attachment site, the free loops, the abdomen attachment site, and beside the fetal urinary bladder [Figure 3].

Besides, the bladder's right and left umbilical arteries were sampled separately, and average values were considered for calculation [Figure 4]. Once we obtained the waveforms at these sites, RI and PI values were taken by manual tracing. In this study, we mainly consider RI and PI values, which were angle independent, although the Doppler angle was kept below 30° to obtain more accurate Doppler values.

RESULTS

We enrolled 312 pregnant females who fulfilled the inclusion criteria in the study period.

The maximum number of cases was in 32 ± 1 week of gestation, and the minimum number of patients were 30 ± 1 week of pregnancy [Figure 5].

In our study, we noticed that UA PI and RI gradually reduce as gestation age progressed, which was maximum at 30 weeks and minimum at 40 weeks of gestation in all the sampled sites.

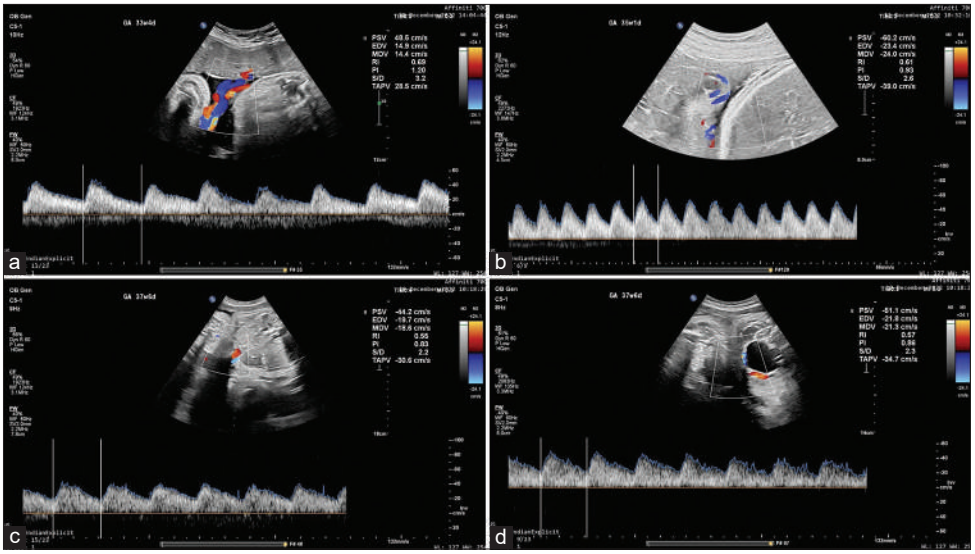

Figure 3: Umbilical artery Doppler wave pattern at different sites. (a) Duplex Doppler ultrasound image of 33-week 4-day fetal umbilical artery sampled at placental attachment site showing normal wave pattern. (b) Duplex Doppler ultrasound image of 35-week 1-day fetal umbilical artery sampled at free loop showing normal wave pattern. (c) Duplex Doppler ultrasound image of 37-week 6-day fetal umbilical artery sampled at abdominal attachment site in axial section showing normal wave pattern. (d) Duplex Doppler ultrasound image of 37-week 6-day fetal umbilical artery sampled beside the bladder in axial section showing normal wave pattern

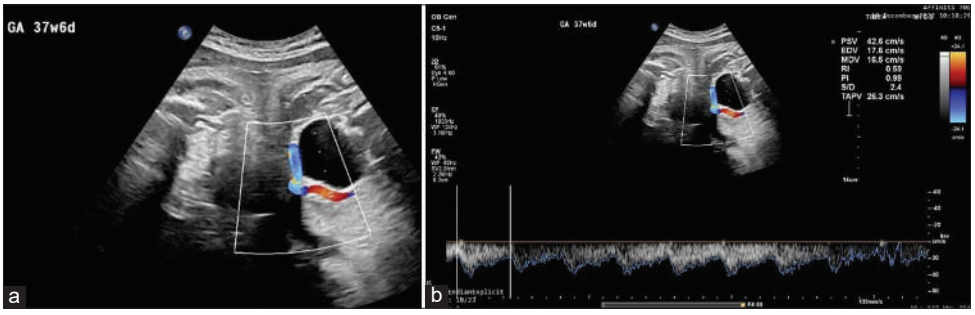

Figure 4: Umbilical artery Doppler sampling beside the fetal urinary bladder. (a) Color Doppler ultrasound image in 37 weeks 6 days fetus in the axial section at the level of bladder showing typical appearance of umbilical artery beside the bladder. In this image, the right uterine artery appears blue, whereas the left umbilical artery is seen in red. (b) Duplex ultrasound demonstrates the umbilical artery wave pattern in the same fetus

In the study, there was a significant difference in the mean RI of the UA with respect to its site. The mean RI of the UA was highest for the left UA beside the urinary bladder (0.68885 ± 0.0815) and lowest for UA at the placental attachment site (0.634 ± 0.0763) [Figure 6].

Bonferroni Test

Umbilical artery RI sampling site	Group based on site of umbilical artery	*P*-value
Umbilical artery RI at placental attachment site	Umbilical artery RI in free loop	0.845
	Umbilical artery RI at abdominal attachment site	0.961
	Right umbilical artery RI at bladder	<0.001*
	Left umbilical artery RI at bladder	<0.001*
Umbilical artery RI in free loop	Umbilical artery RI at abdominal attachment site	1.000
	Right umbilical artery RI at bladder	<0.001*
	Left umbilical artery RI at bladder	<0.001*
Umbilical artery RI at abdominal attachment site	Right umbilical artery RI at bladder	<0.001*
	Left umbilical artery RI at bladder	<0.001*
Right umbilical artery RI at bladder	Left umbilical artery RI at bladder	1.000

There was significant difference in mean RI between the placental and both umbilical arteries beside the bladder.

A significant difference was observed in mean RI between UA in free loop and both umbilical arteries beside the bladder.

There was also a significant difference in RI between UA at abdominal attachment and both umbilical arteries sampled beside the bladder.

In the study, there was a significant difference in the mean PI of the UA with respect to its site. The mean PI of the UA was highest for the right UA beside the fetal urinary bladder (1.072 ± 0.232) and lowest for UA at the placental attachment site (0.975 ± 0.189) [Figure 7].

Umbilical artery sampling site.	Group Based on Site of Umbilical artery	P value
Umbilical Artery PI at Placenta	Umbilical Artery PI in Free Loop	0.328
	Umbilical Artery PI at Abdominal Attachment Site	1.000
	Right Umbilical Artery PI at Bladder	<0.001*
	Left Umbilical Artery PI at Bladder	<0.001*
Umbilical Artery PI in Free Loop	Umbilical Artery PI at Abdominal Attachment Site	1.000
	Right Umbilical Artery PI at Bladder	<0.001*
	Left Umbilical Artery PI at Bladder	0.001
Umbilical Artery PI at Abdominal Attachment Site	Right Umbilical Artery PI at Bladder	<0.001*
	Left Umbilical Artery PI at Bladder	<0.001*
Right Umbilical Artery PI at Bladder	Left Umbilical Artery PI at Bladder	1.000

*--- P-value is statically significant.

There was a significant difference in mean PI between the placental attachment site and both umbilical arteries beside the bladder.

A significant difference was observed in mean PI between UA in free loop and both umbilical arteries beside.

There was also a significant difference in PI between UA at abdominal attachment and both umbilical arteries beside the bladder.

DISCUSSION

The present study was a prospective study which was carried out at the KIMS in Bangalore on 312 pregnant females. Maximum numbers of cases were in 32 ± 1 weeks of gestation, and the minimum number of cases was 30 ± 1 week of gestation.

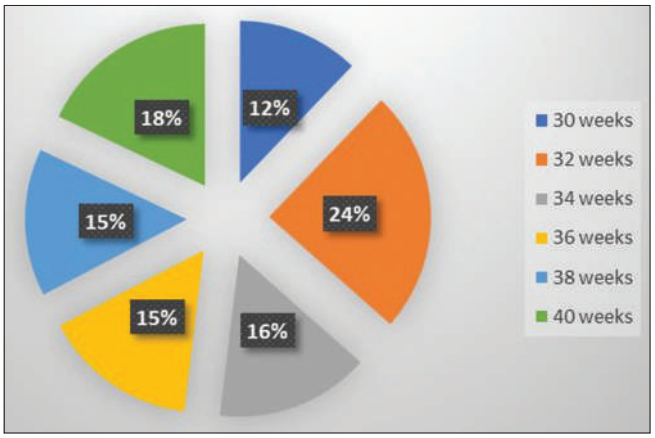

Figure 5: Distribution of gestational age

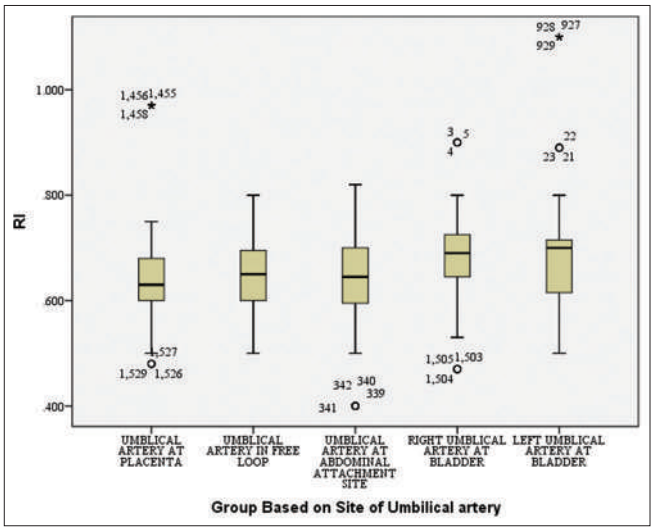

Figure 6: Box plot showing RI of umbilical artery with respect to different sites

In our study, the UA PI and RI values showed a gradual decline throughout the gestation [Table 1].

Srikumar *et al*.[4] (2017) study showed that fetal middle cerebral artery (MCA) and UA Doppler indices followed a definite pattern depending on the gestational age. The UA PI and RI showed a gradual decline throughout the gestation, likely due to a decrease in placental resistance as the pregnancy progressed.

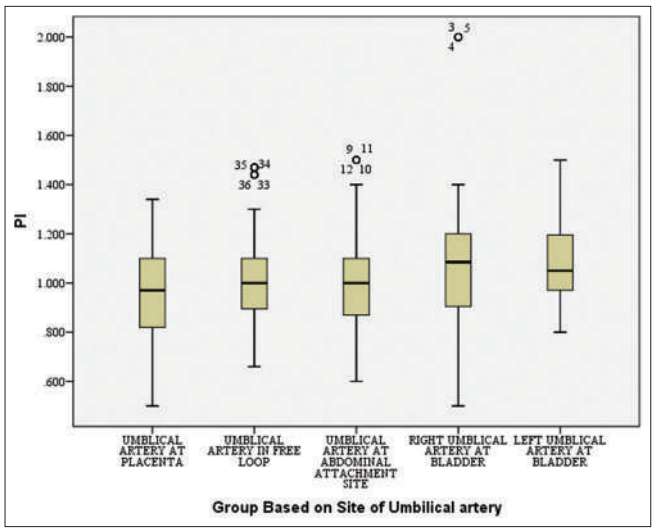

Figure 7: Box plot showing PI of umbilical artery with respect to different sites

Our study showed a significant difference in the mean RI of the UA with respect to its site. The mean RI of the UA was highest for Left UA beside the urinary bladder (0.68885 ± 0.0815) and lowest for UA at the placental attachment site (0.634 ± 0.0763) [Table 2].

There was a significant difference in mean RI and PI between the placental attachment site and both (right and left) umbilical arteries beside the fetal urinary bladder; UA RI in free loops and both (right and left) umbilical arteries beside the fetal urinary bladder; UA at abdominal attachment; and both (right and left) umbilical arteries beside the fetal urinary bladder.

Our study showed a significant difference in the mean PI of the UA with respect to its site. The mean PI of the UA was highest for the right UA beside the fetal urinary bladder (1.072 ± 0.232) and lowest for UA at placental attachment (0.975 ± 0.189) [Table 3].

Trudinger attributed the difference in a gradient from the fetal to the placental ends of the cord entrance region phenomenon.[5] The decrease may also be because of the

Table 1: RI and PI values with respect to gestational age at different sites

Umbilical artery sampling site	Gestational age											
	30 weeks		32 weeks		34 weeks		36 weeks		38 weeks		40 weeks	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Umbilical artery RI at placental attachment site	0.64	0.06	0.65	0.09	0.63	0.08	0.64	0.08	0.62	0.06	0.62	0.08
Umbilical artery RI in free loop	0.67	0.06	0.65	0.06	0.65	0.07	0.64	0.06	0.65	0.05	0.63	0.07
Umbilical artery RI at abdominal attachment site	0.65	0.09	0.65	0.07	0.64	0.09	0.63	0.08	0.66	0.06	0.64	0.07
Right umbilical artery RI at bladder	0.69	0.09	0.69	0.07	0.68	0.08	0.69	0.08	0.69	0.07	0.67	0.08
Left umbilical artery RI at bladder	0.70	0.11	0.69	0.08	0.70	0.10	0.67	0.10	0.71	0.11	0.67	0.08
Mean RI of right and left umbilical artery	0.69	0.09	0.69	0.06	0.69	0.08	0.68	0.07	0.70	0.08	0.67	0.06
Umbilical artery PI at placenta	1.00	0.19	0.99	0.18	0.98	0.18	0.98	0.18	0.96	0.22	0.94	0.19
Umbilical artery PI in free loop	1.05	0.17	1.03	0.17	1.03	0.20	0.98	0.17	1.02	0.18	0.95	0.17
Umbilical artery PI at the abdominal attachment site	1.03	0.24	1.00	0.17	0.98	0.16	0.98	0.14	1.02	0.16	0.97	0.15
Right umbilical artery PI at bladder	1.12	0.24	1.08	0.24	1.05	0.22	1.09	0.27	1.05	0.17	1.05	0.23
Left umbilical artery PI at bladder	1.09	0.19	1.08	0.17	1.09	0.18	1.04	0.19	1.05	0.14	1.06	0.17
Mean PI of right and left umbilical artery	1.10	0.18	1.07	0.15	1.06	0.15	1.05	0.17	1.05	0.14	1.04	0.15

PI: Pulsatility index, RI: Resistivity index

Table 2: Mean RI of umbilical artery at different sites

Umbilical artery sampling site	*n*	Mean	SD	95% Confidence interval for mean		Minimum	Maximum	*P*-value
				Lower bound	Upper bound			
RI								
Umbilical artery RI at placenta	312	0.63415	0.07638	0.62563	0.64267	0.480	0.970	<0.001*
Umbilical artery RI in free loop	312	0.64500	0.06327	0.63795	0.65205	0.500	0.800	
Umbilical artery RI at abdominal attachment site	312	0.64462	0.07702	0.63604	0.65320	0.400	0.820	
Right umbilical artery RI at bladder	312	0.68481	0.07811	0.67611	0.69351	0.470	0.900	
Left umbilical artery RI at bladder	312	0.68885	0.09432	0.67834	0.69935	0.500	1.100	
Total	1560	0.65950	0.08157	0.65545	0.66355	0.400	1.100	

PI: Pulsatility index, RI: Resistivity index, * P-value is statically significant

Table 3: Mean PI of umbilical artery at different sites

Umbilical artery sampling site	*n*	Mean	SD	95% Confidence interval for Mean		Minimum	Maxim um	*P*-value
				Lower bound	Upper bound			
PI								
Umbilical artery PI at placenta	312	0.975	0.189030	0.95466	0.99685	0.500	1.34	<0.001*
Umbilical artery PI in free loop	312	1.0082	0.177449	0.98850	1.02804	0.660	1.47	
Umbilical artery PI at abdominal attachment site	312	0.995	0.170117	0.97701	1.01491	0.600	1.50	
Right umbilical artery PI at bladder	312	1.0721	0.232838	1.04618	1.09805	0.500	2.00	
Left umbilical artery PI at bladder	312	1.0694	0.173221	1.05013	1.08872	0.800	1.50	
Total	1560	1.0243	0.193731	1.01471	1.03396	0.500	2.00	

PI: Pulsatility index, RI: Resistivity index

dampening and attenuation of the propagated wave. Other suggested possibilities are changes in elasticity in the walls of the vessels or changes in the diameter of these vessels. A computer model used for studying the difference in RI from fetal to the placental site showed that placental resistance was a primary factor determining the differences, whereas the viscosity of the blood and cord length were secondary factors.[6]

The changing gradient along the umbilical cord length means that UA Doppler indices will vary depending on the site of insonation. The free loops are the most commonly used site in clinical practice, as it is technically easier to obtain, but it is likely to have significant inter- and intraobserver variability because sampling could be from very disparate sites. These differences are likely to be more marked where the waveform and indices are abnormal. Abramowicz *et al*., for example, examined differences in the indices at the two fixed sites (placental and abdominal attachment) and reported that normal values were obtained for S/D at the placental site when simultaneous examination of the fetal abdominal site obtained highly abnormal values.[7]

Friedman *et al*.[8] recommended measuring the S/D ratio at the insertion of the cord to improve reproducibility, but these sites are often technically challenging to insonate, especially at the later stages of pregnancy due to a poor angle of insonation, the relationship of the fetus with the placenta, or oligohydramnios/anhydramnios.

CONCLUSION

Our findings of varying Doppler indices depending on the UA sampling site have significant implications for clinical practice in monitoring fetuses for further management.

Whenever UA Doppler indices are abnormal, the site of sampling will be an essential variable in determining the degree of abnormality and timing of the delivery.

For this reason, it is essential to monitor fetal well-being by assessment at a constant site for UA Doppler so that the variability will be less and can be clinically correlated with different outcomes.

Whenever we encounter any difficulty in locating a fixed place for monitoring, we can alternatively conduct the UA sampling next to the fetal urinary bladder, like in cases of monoamniotic twins where the investigation of individual fetuses can be undertaken confidently; severe growth restriction with severe oligohydramnios or anhydramnios or ruptured membranes with associated oligohydramnios.

It is time for radiologists to consider defining a reference point for the UA Doppler. This will ensure comparisons of results, consistency in interpretation, and further monitoring.

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Original Article

Assessing the Pre-operative and Intraoperative Factors Responsible for the Conversion of Laparoscopic Cholecystectomy to Open Cholecystectomy: A Retrospective Study

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ABSTRACT

Background: Gallstones are a very common disease, the incidence of which has been increasing progressively over the past few years. The treatment of gallbladder stones when symptomatic consists of cholecystectomy, which is the surgical procedure in which the gallbladder, along with its contents, is removed.

Purpose: The purpose of this study was to determine the rate of conversion of laparoscopic cholecystectomy to open cholecystectomy and to identify the pre-operative and intraoperative factors responsible for the conversion of laparoscopic cholecystectomy to open cholecystectomy.

Materials and Methods: This is a retrospective study conducted in the department of general surgery, KIMS Hospital and Research Center, Bengaluru. Patients who have undergone cholecystectomy from June 2021 to June 2022 for a period of 12 months were selected, and all the relevant history, clinical, laboratory, and intraoperative findings were collected from patient medical record books.

Results: The rate of conversion of laparoscopic cholecystectomy to open cholecystectomy in our study is 20%. The main reasons for conversion are adhesions and bleeding. Significant associated factors are male gender, T2 diabetes mellitus, and intraoperative complications.

Conclusion: The present study showed that gallstone diseases were more common in females than in males. Diabetic patients have shown a higher rate of conversion than non-diabetic patients. (1) Ultrasonography is the most economical, simplest, easiest, and initial tool for the evaluation of gallstone diseases presence of adhesions and inflammation intraoperatively is a key factor, and (2) the rate of conversion and the bile stone spillage is proportional to the severity of the disease.

Key words: Laparoscopic cholecystectomy, Open cholecystectomy, Cholelithiasis

INTRODUCTION

Gallstones are a very common disease the incidence of which has been increasing progressively over the past few years.[1] The treatment of gallbladder stones when symptomatic consists of cholecystectomy, which is the surgical procedure in which the gallbladder along with its contents is removed.

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The past cholecystectomy was done by open surgeries that were associated with the very high morbidity.[2]

To gain access to the gallbladder in case of open surgeries, layers of abdominal wall muscles had to be incised and then resutured also so it was associated with the long post-operative recovery period and at times complicated by post-operative complications such as right-sided pleural effusion, collection in the advent surgical site infection, and others.[3,4]

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The past few years has seen a dramatic change in the way cholelithiasis that has been treated especially with symptomatic with the advent of invasive surgery is such as laparoscopic surgery, single-incision laparoscopy, multiport laparoscopy, and robotic surgery the popularity and mortality associated with open surgery has been reduced drastically also better training facilities unlike diverse and a better understanding has decreased significantly the learning curve that was associated with mortality and morbidity in the past due to which laparoscopy was kept at bay.[5-9]

It has been more than two decades since Kerman performed the first cholecystectomy in north America and 17 years since laparoscopic cholecystectomy was deemed equal to open cholecystectomy in a consensus statement by the national institute of health (NIH).[10] Today, laparoscopic cholecystectomy has become the procedure of choice for symptomatic biliary disease. Approximately 75% of all cholecystectomies are performed laparoscopically and conversion to open procedure ranges from 5% to 10% worldwide.[11]

The initial studies showed that in the cases, when laparoscopic approach was used to remove the gallbladder the rate of complication was 5 times higher than the open method with injury to the CBD being the most common.

This had been improved and reduced over the years as a result of judicious use of cholangiography in the intraoperative period and with gaining increasing experience and familiarity in the laparoscopic anatomy with the rates of the injury to the CBD reducing between 0.25% and 0.5%.

The most important thing is that in with the advent of laparoscopy, there has been a significant decrease in the post-operative recovery period and return to work as a result of reduction in the post-operative pain. This has also reduced the DALY and hence improved economy to the patient.

In this study, we sought to assess our experience with laparoscopic cholecystectomy focusing on patient specific factors that may be associated with a higher rate of conversion over a 12 months study period.

With all the above said, we decided to evaluate the rate of conversion from laparoscopic cholecystectomy to open cholecystectomy and the various factors that contributed toward the conversion. The study was undertaken so that the factors can be evaluated thoroughly and the rate of conversion reduced that can in turn affect morbidity associated with open surgeries can be reduced.

Aims and Objectives of the Study

The aims of this study were as follows:

1. To determine the rate of conversion of laparoscopic cholecystectomy to open cholecystectomy.
2. To identify the pre-operative and intraoperative factors responsible for conversion of laparoscopic cholecystectomy to open cholecystectomy.

MATERIALS AND METHODS

Study Design

This study was a retrospective study.

Study Subjects

- All patients who had presented with cholelithiasis and with no contraindication during the study period were included in the study.
- Medical records of all patients who had undergone laparoscopic cholecystectomy during the study period were reviewed.
- The data recorded included demographic information, past medical history, indication for operation, duration of operation, the reason for conversion, and post-operative complication.

Source of Data

This study was conducted in the Department of General Surgery, Kempegowda Institute of Medical Sciences and Research Center. We have included patients who had undergone laparoscopic cholecystectomy from June 2021 to June 2022 for a period of 12 months.

Sampling Method and Sampling Size

The name and patient ID were recorded and anonymity was achieved, patients were given random computer-generated numbers.

Inclusion Criteria

The following criteria were included in the study:

- All patients with symptomatic cholelithiasis (including acute cholecystitis)
- Patients presenting with acalculous cholecystitis.
- Age >18 years.

Exclusion Criteria

The following criteria were excluded from the study:

- Carcinoma of gallbladder.
- Perforated gallbladder.
- Patients unfit for general anesthesia.
- Previous upper abdominal surgeries.
- Age < 18 years.

Methodology

The patients who were chosen and gave an informed consent following details were recorded:

- Name: -
- Age: -
- Sex: -
- Random number: -
- Address: -
- Religion: -
- Date of admission: -
- Date of surgery: -
- Date of discharge: -
- Chief complaints: -
- History of presenting illness: -
- Past history: -
- Family history: -
- General physical examination: -
- Systemic examination: -

Investigation

- Complete blood count: -
- Blood sugar: -
- Renal function test: -
- Liver function test: -
- Hepatitis status: -
- Chest X-ray: -
- Ultrasound of abdomen: -

Number of calculus: -
Size of calculus-
Gallbladder wall thickness: -
Pericholecystic collection: -
CBD calculi: -
Dilatation of CBD: -

Surgery

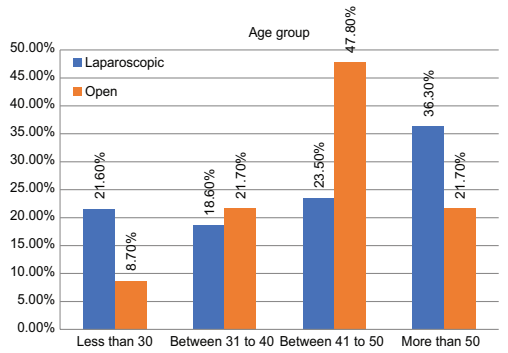
- Date of surgery:-
- Age of patient: -
- Intraoperative findings: -
- Duration of surgery: -
- Cause of conversion: -

Adhesion: Yes/no
Hemorrhage: Yes/no
Organ injury: Yes/no
Other causes.

RESULTS

This study was conducted in the Department of General Surgery, KIMS Hospital and Research Center, Bengaluru. We have included patients who had undergone laparoscopic cholecystectomy from June 2021 to June 2022 for a period of 12 months.

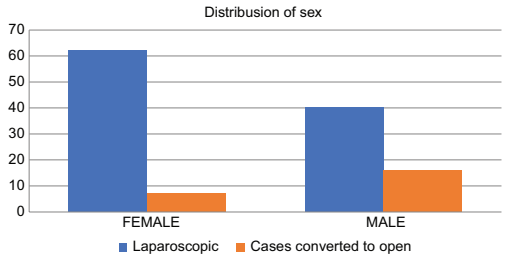
Age Distribution of the Cases Studied



The mean age of the cases studied was 44.92 years, SD = 15.29 years in laparoscopic cholecystectomy with >50 years being the most common age with 37 cases 36.3%, followed by 41–50 years with 24 cases 23.5%, <30 years with 22 cases 21.6%, 31–40 years with 19 cases 18.6%, and mean age in cases converted to open cholecystectomy is 46.65 years, SD = 11.44 years, 41–50 years with 11 cases 47.8%, 31–40 years and >50 years with five cases each 21.7%, and <30 years two cases with 8.7%.

Gender Distribution of the Cases Studied

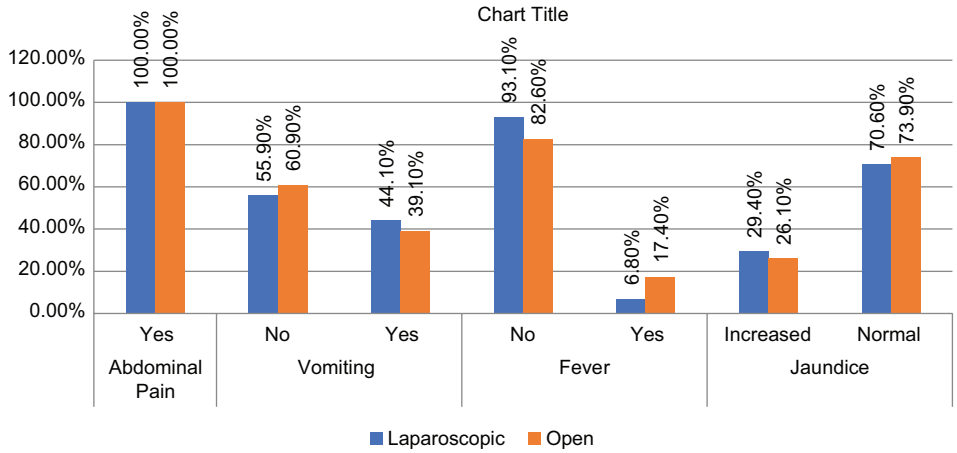
The most common gender that required cholecystectomy was the female gender, with 69 cases with 60.8% in laparoscopy cholecystectomy and 16 cases with 69.6% which were converted to open cholecystectomy with $P = 0.0432$ which is statistically significant.



Symptomatology of the Cases Studied

Symptoms	Laparoscopic		Cases converted to open	
	Count	N (%)	Count	N (%)
Abdominal pain				
Yes	102	100.0	23	100.0
Vomiting				
No	57	55.9	14	60.9
Yes	45	44.1	9	39.1
Fever				
No	95	93.1	19	82.6
Yes	7	6.8	4	17.4
Jaundice				
Increased	30	29.4	6	26.1

All 125 cases (100%) presented with abdominal pain in the right upper abdomen.



About 45 (44.1%) patients had vomiting in the laparoscopic cholecystectomy group and 9 (39.1%) in conversion to open cholecystectomy group with $P = 0.663$ 7 (6.8%) patients had fever in laparoscopic group and 4 (17.4%) in conversion to open cholecystectomy group with $P = 0.107$.

Thirty (29.4%) patients had jaundice in the laparoscopic group and 6 (26.1%) in open cholecystectomy converted group with $P = 0.750$.

Investigations

Investigations	Laparoscopic		Cases converted to open	
	Count	Column N (%)	Count	Column N (%)
HB normal or				
Normal	93	91.2%	23	100.0%
Reduced	9	8.8%	0	0.0%
TC elevated				
Elevated	45	44.1%	6	26.1%
Normal	57	55.9%	17	73.9%
TB elevated or not				
Elevated	12	11.8%	5	21.7%
Normal	90	88.2%	18	78.3%
SGOT elevated or not				
Elevated	19	18.6%	2	8.7%
Normal	83	81.4%	21	91.3%
SGPT elevated or not				
Elevated	18	17.6%	2	8.7%
Normal	84	82.4%	21	91.3%
Blood urea				
Increased	9	8.8%	1	4.3%
Normal	93	91.2%	22	95.7%
S. Creatinine				
Increased	8	7.8%	1	4.3%
Normal	94	92.2%	22	95.7%

Hemoglobin is reduced in 9 (8.8%) in laparoscopic cholecystectomy group with $P = 0.139$. Total counts is elevated in 45 (44.1%) in laparoscopic cholecystectomy group and 6 (26.1%) in open cholecystectomy group with $P = 0.112$. Mean Hb is 12.41 g/dL with SD of 1.83 in the laparoscopic group and mean Hb is 12.65 and SD 1.61 in open converted group with mean of 9787.80 and SD 3556.60 in laparoscopic group and mean of 8396.61 and SD of 3169.05 in open cholecystectomy group.

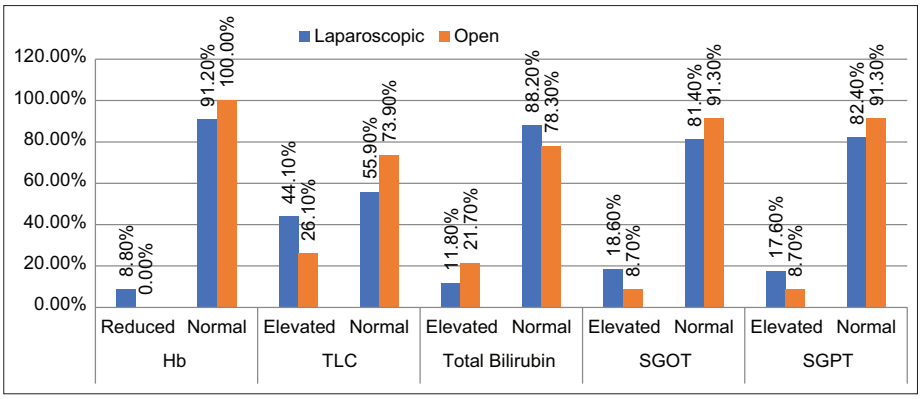
Investigations	Laparoscopic		Cases converted to open	
	Mean	Standard deviation	Mean	Standard deviation
HB%	12.41	1.83	12.65	1.61
TC	9787.80	3556.60	8396.61	3169.05
TB	0.48	0.70	0.57	0.90
SGOT	30.06	31.61	22.00	11.07
SGPT	30.08	40.52	19.00	10.46
FBS	116.19	51.07	127.48	53.38
PPBS	129.86	52.89	143.70	45.57

Total bilirubin is elevated in 12 (11.8%) in laparoscopic cholecystectomy and 5 (21%) in open converted cases with a significant $P = 0.207$ with mean of 0.48 and SD = 0.70 in laparoscopic group and mean of 0.57 and SD of 0.90 in open cholecystectomy group.

SGOT is elevated in 19 (18.6%) in laparoscopic cholecystectomy and 2 (8.7%) and in open conversion cases with $P = 0.250$ with mean of 30.06 and SD = 31.61 in laparoscopic group and mean of 22.00 and SD 11.07 in open cholecystectomy group. SGPT is elevated in 18 (17.6%) in laparoscopic cholecystectomy group and 2 (8.7%) and in open cholecystectomy group with $P = 0.290$ with mean of 30.08 and SD = 40.52 in laparoscopic group and mean of 19.00 and SD 10.46 in open cholecystectomy group.

Mean FBS is 116.19 and SD is 51.07 in laparoscopic group, mean of 127.48, SD = 53.38 in open conversion group with $P = 0.344$.

Mean PPBS is 129.86, SD is 52.89, in laparoscopic group and mean of 143.70, SD of 45.57 in open converted cases with $P = 0.210$.

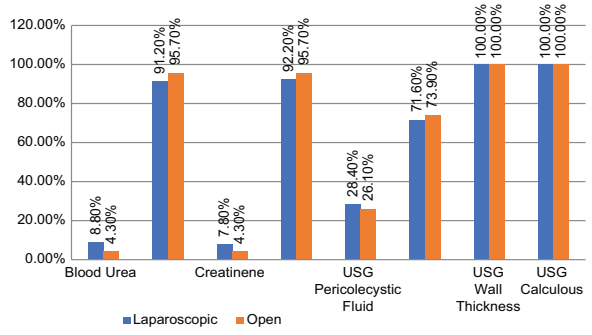


Blood urea is increased in 9 (8.8%) in laparoscopic cholecystectomy group and 1 (4.3%) with a $P = 0.475$. S. Creatinine is increased in 8 (7.8%) in laparoscopic cholecystectomy and 1 (4.3%) in open conversion cases with $P = 0.558$.

Radiological Investigations

Radiological findings	Laparoscopic		Cases converted to open	
	Count	Column N (%)	Count	Column N (%)
USG pericholecystic fluid				
Absent	29	28.4%	6	26.1%
Present	73	71.6%	17	73.9%
USG wall thickness				
Present	102	100.0%	23	100.0%
USG calculous				
Present	102	100.0%	23	100.0%

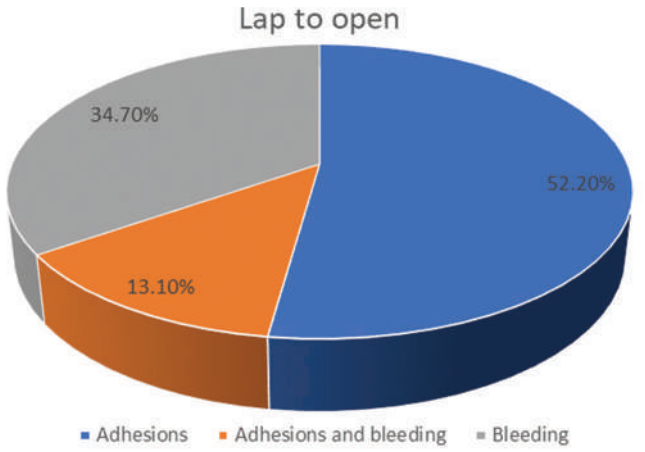
On USG, pericholecystic fluid was noted in 73 (71.6%) patients in laparoscopic cholecystectomy and 17 (73.9%) patients in conversion to open cholecystectomy. Gallbladder wall thickness was increased in 102 patients in laparoscopic cholecystectomy group and 23 patients in open conversion group and calculous is noted in 102 patients in laparoscopic group and 23 patients in open conversion group.



Intraoperative Factors Leading to Laparoscopic to Open Conversion

Out of 125 patients, 12 (9.6%) patients had dense adhesions to adjacent structures (omentum, stomach and duodenum) [Figure 1], 3 (2.4%) had adhesions and bleeding [Figures 2 and 3], and 8 (6.4%) had only bleeding, which are the important intraoperative factors responsible for the conversion of laparoscopic to open cholecystectomy.

Conversion of cases to open cholecystectomy	Count	Column N (%)
Why converted in to lap		
Adhesions	12	9.6%
Adhesions and bleeding	3	2.4%
Bleeding	8	6.4%
NA	102	81.6%



DISCUSSION

Laparoscopy has come that an extensive way since it originated; over the past few decades, rapid advances have made laparoscopic surgery very feasible. The laparoscopic cholecystectomy has become the gold standard treatment for management of gallbladder diseases. Conversion to open cholecystectomy sometimes becomes and a number of factors play a role in it and by identifying them it will help in proper patient selection and also make the operating surgeon to identify the possible candidates who may need conversion so that the required back up such as anesthetic drugs, the blood, and the support staff be ready. In our

study, we found the following in comparison to other studies.

Comparison of the Significance of Gender

Conversion of cases to open cholecystectomy	The gender of the cases studied		Total
	M	F	
Converted to open			
No	62	40	102
Yes	7	16	23
Total	78	69	56

There was a significant difference in the gender with the male gender being at a higher risk of conversion to open with $P = 0.0432$, which is statistically significant [Table 1].

Hutchinson *et al.*, Liu *et al.,* and Ibrahim *et al.*[12] stated that male gender was a predictor for conversion. Jeremy demonstrated that significant independent predictive factors for conversion of laparoscopic cholecystectomy to open cholecystectomy were male gender.

There was a significant difference in the BMI with the male gender being at a higher risk of conversion to open with $P = 0.001$ [Table 2].

Hutchinson *et al.* and Liu *et al.*[13] patients with a body mass index >27.2 kg/m^2 needed conversion, Thami *et al.* in a prospective study in the year 2018 in India in 200 patients BMI <25 Kg/m,^{2} the conversion rate was 3% and those with BMI >25 Kg/m^2 were 24%.

Age of the Cases Studied

The mean age of the cases studied is 44.92 years, SD = 15.29 years in laparoscopic group. Mean age in open converted group is 46.65 years, SD = 11.44 years. There was no significant difference in the age with the risk of conversion to open with a $P = 0.077$

Conversion of cases to open cholecystectomy	Pain abdomen	Total
	Yes	
Converted to open		
No	102	102
Yes	23	23
Total	125	125

There was no significant difference in the pain abdomen with the risk of conversion to open with $P = 0.663$.

Conversion of cases to open cholecystectomy	Vomiting		Total
	No	Yes	
Converted to open			
No	45	57	102
Yes	9	14	23
Total	54	71	125

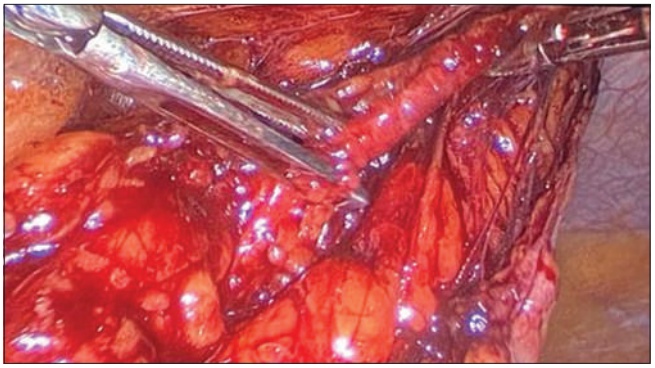


Figure 1: Intraoperative image of laparoscopic cholecystectomy demonstrating omental adhesions

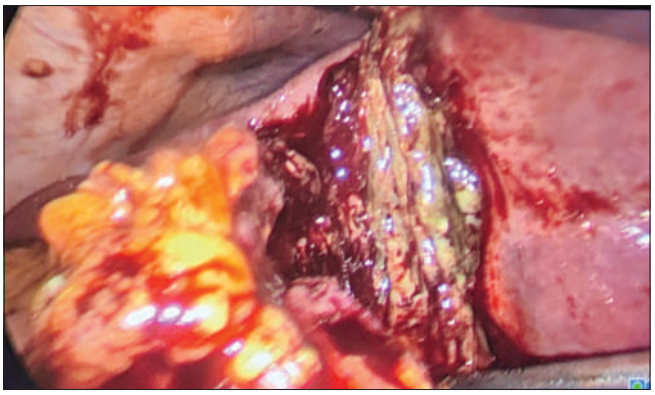


Figure 2: Intraoperative image of laparoscopic cholecystectomy showing intractable bleeding during adhesiolysis, hence converted to open cholecystectomy

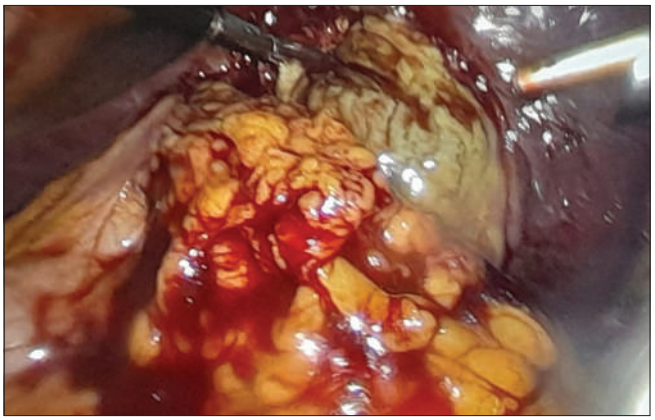


Figure 3: Intraoperative image of laparoscopic cholecystectomy showing adhesion of the omentum and duodenum to the gangrenous gallbladder, therefore converted toopen cholecystectomy

Table 1: Gender of the cases studied

Gender	Laparoscopic		Cases converted to open	
	Count	Column N (%)	Count	Column N (%)
Gender				
Female	62	60.8	7	30.4
Male	40	39.2	16	69.6

Table 2: Age of the cases studied

Age group	Laparoscopic cholecystectomy		Open cholecystectomy		Chi-square test
	Count	Column N%	Count	Column N%	
Less than 30	22	21.6	2	8.7	Chi-square=6.852
Between 31 to 40	19	18.6	5	21.7	P=0.077
Between 41 to 50	24	23.5	11	47.8	
More than 50	37	36.3	5	21.7	

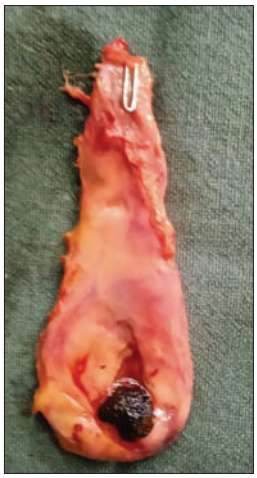
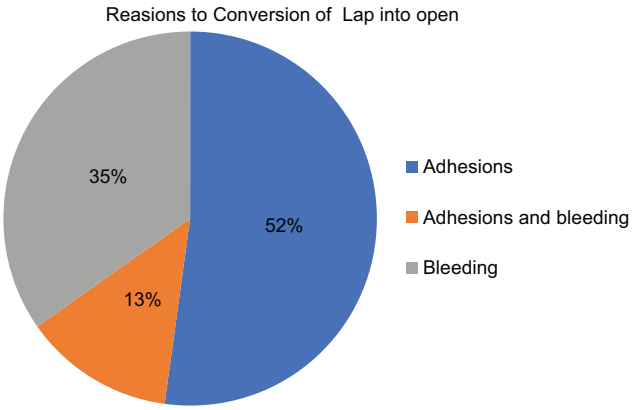


Figure 4: Gallbladder specimen post-cholecystectomy showing single calculous, with features of acute cholecystitis



FEVER	Fever		Total
	Yes	No	
Converted to open			
No	95	7	102
Yes	4	19	23
Total	99	26	125

JAUNDICE	Jaundice		Total
	Yes	No	
Converted to open			
No	72	30	102
Yes	17	6	23
Total	89	36	125

There was no significant difference in the vomiting with the male gender being at a higher risk of conversion to open with p value 0.663.

Converted to Open FEVER Cross Tabulation

There was no significant difference in the fever with the risk of conversion to open with $P = 0.107$.

Converted to Open *Jaundice Cross Tabulation

There was no significant difference in the jaundice with the risk of conversion to open with $P = 0.750$.

In all, 125 cases (100%) had cholelithiasis that was the USG findings.

Lipman *et al.*,[14] demonstrated that significant independent predictive factors for conversion of laparoscopic cholecystectomy to open cholecystectomy were thickened gallbladder wall [Figure 4] on preoperative ultrasonography of abdomen.

Reason to Conversion of Laparoscopic to Open Cholecystectomy

Total cases converted to open	Adhesion	Adhesions and bleeding	Bleeding
23	12	03	08

The rate of conversion was 20% in our study.

Faruquzzaman *et al.* in the year 2015 in a study that was done on five hundred cases that had planned for laparoscopic cholecystectomy in two different hospitals stated that the rate of conversion of laparoscopic to open cholecystectomy was 5.2% and 7.0%.

Le *et al.*[15] in the year 2012 in stated that the rate of conversion of laparoscopic to open cholecystectomy was 2.6%.

Vishnuvarthan[16] in a prospective study in the year 2018 in Tamil Nadu, India, found that 13 of the 98 were converted to open cholecystectomy with the rate being 13.26%.

CONCLUSION

The present study of 125 patients has shown that gallstone diseases were more common in females than to males with a ratio.

Diabetic patients have shown a higher rate of conversion than non-diabetic patients.

- Ultrasonography is the most economical, simplest, and easiest and an initial tool for the ϖ evaluation of gallstone diseases. Presences of adhesions and inflammation intraoperatively iare key factor,
- The rate of conversion and the bile stone spillage is proportional to the severity of the disease.

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Original Article

Influence of Betelnut Chewing and its Correlation with Pulp stone among Adult Rural Population of Sullia Taluk, Dakshina Kannada District: A Retrospective Study

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Abstract

Background: Globally approximately 600 million people practice the habit of betel nut chewing. In Dakshina Kannada, betel nut is consumed as a major constituent mixed with or without various tobacco products. Its use is acceptable among all sections of society, including women and children. Pulp stones are discrete calcified stones or foci of calcification in the dental pulp. The exact causes of pulp stones are unclear, but they are often found in patients consuming these products. To date, there is no literature, which determines the association between betelnut chewing and pulp stones in the Dakshina Kannada population.

Aim: The aim of the study was to determine the correlation between betelnut chewing and pulp stones in comparison with those of healthy subjects without any betel quid chewing in rural population of Dakshina Kannada district, Karnataka, India.

Materials and Methods: A total of 100 patient records were examined, comprising of patients with betel nut chewing and control group. The teeth were examined under ×2 magnification on orthopantomography. The presence or absence of pulp stones was recorded.

Statistical Analysis: All statistical analyses were performed using the SPSS software. For each variable, the mean and standard deviation were calculated. Analysis of the data between groups was carried out by paired and unpaired *t*-tests.

Results: The study sample included 2798 teeth identified in full mouth series of orthopantomography of patients aged between 20 and 55 years. Pulp stones were found in 13.35% of the total teeth examined. When compared to teeth type and pulp stones, first molar showed increased prevalence of pulp stones.

Conclusion: A positive correlation was found between patients with betel nut chewing and pulp stones. The findings suggest that the constant masticatory forces by the virtue of chewing betel quid leads to the formation of pulp stones.

Key words: Betel quid, Endodontic treatment, Occlusal forces, Pulp stone, Rural population

INTRODUCTION

Approximately 600 million people practice the habit of betel nut chewing (Gupta and Warnakulasuriya 2002). The areca nut is the seed of the areca palm, commonly referred to as betel nut.[1] Usually, betel is consumed as betel quid; a small package containing pieces of betel nut and slaked lime (calcium hydroxide) wrapped in a betel leaf. Betel quid chewing results in overall reddish staining of the teeth due to the tannin present in the arecanut. Due to its mild stimulating effects, it is most often used as a recreational drug, but it is also part of rituals and traditional medicine (Zumbroich 2008).[2] The origin of betel nut chewing in Southeast Asia can be traced back for more than 2000 years by historical, linguistic, and ethnographic sources.

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Biochemically, the active tetrahydropyridine alkaloids of the betel nut (arecoline, arecaidine, guvacoline, and guvacine) can be detected in high concentrations in saliva (Franke *et al*. 2015).[3] During mastication with slaked lime, the ester bonds of arecoline and guvacoline are cleaved, yielding arecaidine, and guvacine, respectively. Habitual use can lead to permanent staining of all enamel surfaces. The hard fibrous nature of the betel nut can lead to fractured teeth and extensive attrition of the occlusal tooth surface among regular users. The loss of enamel may also expose the underlying dentine which may result in dentinal sensitivity. Due to a lack of awareness, chewing betel nuts is one of the most common addictions in India which can result in compromised oral hygiene and esthetics. These are available in the form of several chewing products such as paan, gutka, khaini, and paan masala. Its use is acceptable among all sections of society, including women and quite often in children.[4,5]

Pulp stones are discrete calcified stones or foci of calcification in the dental pulp. Although pulp stones rarely cause pain, they must be evaluated because a tooth undergoing endodontic treatment may be affected clinically by the presence of large pulp stones. Large pulp stones in the pulp chamber blocks the access to the orifices and also deflect or engage the tip of hand or rotary instruments, thereby, preventing its easy passage. The exact causes of pulp stones are unclear, but they are often found in patients consuming these products.[6] Another factor indicated in the literature that contributes to stone formation may be high masticatory forces, manifested through dental wear or through constant chewing habits as quid chewing. Moreover, it could result from ageing, pulp degeneration, circulatory disturbances in pulp, high masticatory forces due to behavioral activities, operative procedures, or orthodontic movements.

The prevalence of pulp stones in teeth, based on radiographic examination, has been reported to be around 20–25% depending on the study type, design, and radiographic technique employed while histological examinations reveal higher percentages.[7] da Silva *et al*. had found that CBCT provides accurate anatomical details in three dimensions, offering the possibility to view an individual tooth in axial, sagittal, and coronal views.[8]

Bernick and Nedelman found with age, pulp chamber size decreases due to the deposition of secondary dentin in the root.[8] As a result of dental caries, pulp inflammation triggers secondary (reparative) dentin formation and calcification. To date, there is no literature, which determines the association between betelnut chewing and pulp stones in the Dakshina Kannada population.

MATERIALS AND METHODS

A total of 3092 teeth were evaluated from 100 panoramic radiographs obtained from the Department of Oral Medicine and Radiology, KVG Dental College, Sullia, Dakshina Kannada, Karnataka.

50 Records with history of betelnut chewing and 50 records of healthy subjects were randomly selected for the study.

Inclusion Criteria

The following criteria were included in the study:

- Fully erupted, minimally restored, non-carious teeth, free from radiographically observable pulpal sclerosis
- Individuals with betel nut chewing habits for more than 3 years duration
- Age group-between 20 and 55 years.

Exclusion Criteria

The following criteria were excluded from the study:

- Teeth with crown or bridge
- Carious lesions and deep restorations
- Patients with syndromes that are more prone to pulp stones.

Evaluation of Panoramic Radiograph

Definite radiopaque body which is found inside the pulp chamber was considered as pulp stones and a score of presence or absence was given after the confirmation by two different examiners [Figure 1].

Statistical Analysis

All statistical analysis was performed using the SPSS software 22. For each variable, a mean and standard deviation was calculated. Analysis of the data between groups was carried out by paired and unpaired *t*-tests.

RESULTS

Tables 1 and 2 show intergroup comparison of patients with betel quid chewing compared to healthy subjects. It is seen that subjects with betel quid chewing had more pulp stone compared to that of healthy subjects. The prevalence of pulp stone based on the tooth type was in the order first molar > second premolar > second molar > first premolar [Figure 2]. Pulp stones appear more frequently in molars than in premolars. A statistically significant difference was seen between the tested groups ($P < 0.05$).

Table 3 shows the prevalence of pulp stones in maxilla and mandible. The result of the present study showed that maxilla had more occurrences of pulp stone compared to mandible. Pulp stones are rarely found in healthy subjects [Figure 3].

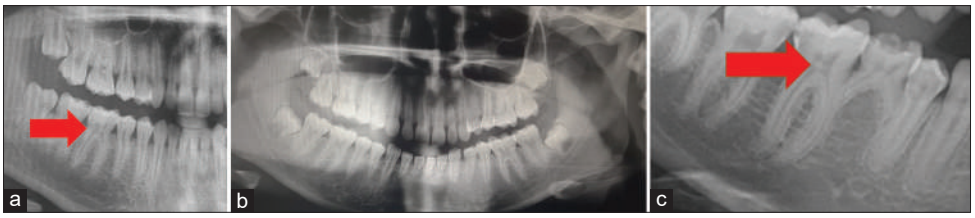

Figure 1: (a-c) The orthopentomograph depicting definite radiopaque body which is found inside the pulp chamber was considered as pulp stones. Scoring was given based on the occurrence of pulp stones

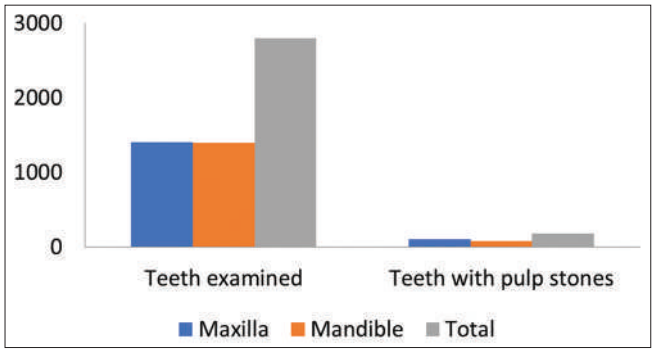

Figure 2: Prevalence of pulp stone in maxilla and mandible

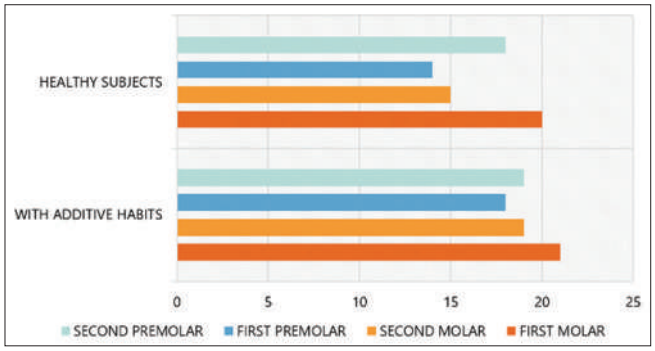

Figure 3: Prevalence of pulp stone based on tooth type

PREVALENCE OF PULPSTONES IN PATIENTS WITH BETEL QUID CHEWING		
	Teeth examined	Teeth with pulp stones
Maxilla	781	53
Mandible	741	42
Total	3092	244

Table 1: Prevalence of pulpstones in patients with betal quid chewing

PREVALENCE OF PULPSTONES IN HEALTHY SUBJECTS		
	Teeth examined	Teeth with pulp stones
Maxilla	706	49
Mandible	704	33
Total	1410	82

Table 2: Prevalence of pulpstones in healthy subjects

PREVALENCE OF PULPSTONES			
	Teeth examined	Teeth with pulp stones	P Value
Maxilla	1403	102	0.06
Mandible	1395	75	
Total	2798	177	

Table 3: Prevalence of pulpstones

DISCUSSION

In India, betelnut chewing being one of the most common addictions that can be due to a lack of knowledge and awareness leading to compromised oral hygiene.[9] The hard fibrous nature of the betel nut can lead to fractured teeth and extensive attrition of the occlusal tooth surface among regular users.[4,5] The loss of enamel may also expose the underlying dentine which may result in dentinal sensitivity. The correlation to pulp stones has been plethoric as opposed to aging, behavioral activities, habits, metabolic imbalance or dysfunction, orthodontic treatment, and traumatic occlusion.[6] Various conditions may cause generalized pulp stones to form in the dentition. These include type I osteogenesis imperfecta, type II dentin dysplasia, Elhers-Danlos syndrome, tumoral calcinosis, Elfin facies syndrome, familial expansile osteolysis, and otodental syndrome.[7] In forensic odontology, radiographic matching of pulp stone configurations, along with other features recorded in dental records, may provide valuable information in the identification of deceased person.[10] The highest numbers of pulp stones, among all the examined groups were evident in patients with betel quid chewing.

Exact etiology for the formation of pulp stone is not known.[6] Another factor indicated in the literature that contributes to stone formation may be high masticatory

forces, manifested through dental wear or through constant chewing habits as quid chewing. Numerous researchers have proven the existence of different rates of dental wear in such conditions (Özdemir, Yavuz, and Erol).[11-15] Stronger dental wear and occurrence of pulp stone may be due to "behavioral activities," such as daily tasks including betel quid chewing.[16-19] Moreover, mechanical defects around the functional active surfaces detected on many teeth could be explained by the behavioral habits of biting or holding hard objects. Studies of Hillmann and Geurtsen, Fatemi *et al*., and Chen and Huang reported higher rate pulpal calcifications in elderly patients with periodontal disease.[20-23] These authors also suggested that the frequency, duration and intensity of chronic irritations being causative factors for such calcifications.[24]

According to study type, design, and radiographic technique, pulp stone prevalence ranges from 8% to 90%. Pulpal calcifications have been investigated by radiographs[9-13] or histological sections.[8] Dental pulp stones, which are bigger than 200 mm can be observed by dental radiographs. The radiographic prevalence is less than histologic studies.[11] Radiographs are the only noninvasive way of evaluating dental pulp stones in clinical researches. But these studies tend to underreport the occurrence of pulpal calcifications. Histological observations are also incomplete in this respect because of a limited number of researches.

Although pulp stones rarely cause pain, they must be evaluated because a tooth undergoing endodontic treatment may be affected clinically by the presence of large pulp stones.[13] It is possible for large pulp stones in the pulp chamber to block access to the canal orifices and to deflect or engage the tip of the exploring instrument, preventing its easy passage down the canal. The use of piezoelectric, ultrasonic, and nickel-titanium rotary instruments permits the removal of pulp calcifications and the negotiation of root canal orifices.[13] In the current study, pulp stones were seen more in molar than premolar. This could be due to increase in the occlusal loading at the molar area.[14,15]

In general, bitewing and periapical radiographs can easily demonstrate the calcifications of the pulp as individual tooth can be clearly identified. Baghdady *et al*.[15] used bitewing radiographs to investigate the prevalence of pulp stones. Hamasha *et al*., Darwazeh *et al*.[25,26] and Tamse *et al*.[28] used both periapical and bitewing radiographs for the identification of pulpstones. They compared the two radiographic techniques and concluded that no significant difference was found between the projections. The present study evaluates the occurrence of pulp stone with digital panoramic radiograph so that teeth involved with calcification in both maxilla and mandible can be ruled out.

A wide variety of pulp stone sizes were found in this study, consisting of small particles up to large calcified bodies that occluded a majority of the pulp chamber. However, the true prevalence is likely to be higher than the figure from this radiographic study, because radiographs are not likely to detect pulp stones <200 μm in diameter.[13] However, radiographs are the only means of evaluating pulp stones non-invasively in clinical studies.[10-14] Radiographic differentiation between pulp stone and pulpal sclerosis (which proceeds later to pulpstones) was demonstrated by "white." He explained that early pulpal sclerosis cannot be demonstrated radiographically. In diffuse pulpal sclerosis, there is generalized calcification which is seen throughout the large area of pulp chamber or canal. However, pulp stones may be seen as a definite single or multiple radiopaque structures within the pulp chamber or root canals.[15] In the present study, panoramic radiograph was used because of its main advantage as it shows both jaws on a single radiographic image. It helps evaluate the entire dentition in a panoramic radiograph for pulp stones retrospectively without exposing the patient again for bitewing. This would be ideal for screening pulpal calcifications. The present study sample included 2798 teeth identified in full mouth series of orthopantomagraph of patients aged between 20 and 55 years. Pulp stones were found in 13.35% of the total teeth examined different studies report varying incidences of pulp stones. According to James *et al*., 56% of permanent teeth have pulp stones. In contrast, Ranjitkar *et al*.[16-19] found pulp stones in 10.1% of teeth examined and Tamse *et al*. showed that 20.7% of the teeth had pulp stones based on radiographic examination

In the present study, pulp stones were more prevalent in molar teeth, especially in the maxillary arch.[8,11,14] This is in accordance with the findings reported by Turkal *et al*., Yosuf *et al*., Sisman *et al*., and Ranjitkar *et al*. In contrast with the observations of the present study, Hamasha *et al*.[18] reported occurrence of pulp stones frequently in the mandibular first molar. Being the first tooth to erupt in the oral cavity, molars bear more occlusal forces leading to early degenerative changes. Rich blood supply in molar can also cause increased calcification is yet another proposed factor. Ranjitkar *et al*.[27] calculated the prevalence of pulp stones in young Australian adults using radiographs and reported that occurrences were rare in premolars (0.4%) but significantly higher in molars (19.7%) and more common in first molars than in second molars and in maxillary first molars than in mandibular first molars. These results are attributed to the fact that molars provide better blood flow, which may contribute to calcification. Higher frequency of pulp stones was reported in maxillary arch compared to mandibular arch, but similar frequency in both arches[20,21] or higher occurrence in mandibular arch have also been reported.[29-34]

CONCLUSION

A positive correlation was found between patients with betel quid chewing habit and pulp stones. The findings suggest that the constant masticatory forces by the virtue of chewing betel quid leads to the formation of pulp stones.

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Original Article

Knowledge and Awareness of Menstrual Cup among Reproductive Women

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Abstract

Background: Menstrual cup (MC) is a more contemporary alternative to sanitary napkins. High-quality medical grade silicone (biodegradable) products have the benefit of reusability and have a potential lifespan of up to 10 years. The present study aimed to assess the knowledge and awareness of MC among reproductive women in India.

Methodology: A cross-sectional survey was conducted, using online questionnaire among the general population. The participants aged between 18 and 45 were included in the study.

Results: Of 325 completed responses, majority were aged between 18 and 25 (38.15%). Majority of the responders used sanitary pad (79.3%) and only 3.69% were using MC. The major source of information about the MC is social media. There is significant difference between the age group less than 35 and >35 in knowledge ($P = 0.001$) and attitude toward MC ($P = 0.001$). Majority of the responders are concerned for leakage, inserting in vagina, and fear of allergies. The reason for non-preference of MC was affordability, accessibility, social taboo, and limited knowledge.

Conclusion: Even though many of the participants were aware of the MC's use, it has not yet been widely accepted. Awareness and knowledge could be improved, as there is a room for improvement, people need to understand about the menstrual hygiene and overcome the social taboo and hesitancy. This can be achieved by addressing the fear factors and creating more awareness campaigns from voluntary organizations and government sectors.

Key words: Acceptance awareness, Menstrual cup, Social taboo

INTRODUCTION

Menstruation is a physiological phenomenon; millions of women globally experience every month. It is a normal biological process. Although it is the most common biological process, in lower- and middle-income countries, due to social issues and lack of guidance maximum of the girl's experience fear, confusion, shame, and discomfort while they try to be accustomed to their monthly period.[1] In developing countries like India, it is subjected to stringent social stigma. Different sanitary products are used by women all across India. Some sanitary products are reusable sanitary pads, disposable sanitary pads, tampons, cloth, period pants, and menstrual cups (MC). MCs are reusable sanitary cups which are made of medical grade silicon, latex, or a thermoplastic isomer. These cups were first patented in the USA and presently almost 100 brands are available and marketed globally.[2] The cups can be reused for about 10 years, although they have a higher 1-time investment in comparison to other sanitary products. They are more environmentally friendly as well. MCs have been available since decades, but their use is limited.

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Menstrual health and hygiene have been a relatively unexplored topic in terms of research studies conducted in India. A really small percentage of studies discussed the usage of MCs specifically. In studies conducted in low- and middle-income countries have shown that among school girls, MCs have received positive responses.[3,4] Preliminary studies of acceptability in low- and middle-income countries suggest cups are a potential option for girls as well as women.[5-8] Preclinical assessments did not show any

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evidence that this product was toxic or mutagenic and no health risks were observed during the post-marketing study in the USA.[9] In a study from UK, 55% of participants indicated a desire to continue using the product due to less leakage during activity, environmentally-friendly design, and its long-term cost-effectiveness.[10] Although acceptability of this product has been reported among different cultures,[11] the evidence suggests that women's views on the MCs are related to sociocultural factors.[12] Menstruation is still considered a taboo in some societies.[11]

The Indian study conducted in Maharashtra, Chhattisgarh, Tamil Nadu among school girls on the menstrual hygiene, reported that nearly 1% of the participants were used MCs. The study highlighted that the accessibility might be one of the reasons for the low usage of the cups.[13] There is a paucity of studies focused on the affordability of MCs and a recent meta-analysis showed that that MCs are a safe option for menstruation management and are being used internationally, perhaps the further studies are needed on cost effectiveness.[14] There is a hesitant to switch to MCs, due to various reasons such as reluctance to change usage pattern, and fear or limited knowledge, among college going students in Udaipur.[15] Perhaps in another study conducted in Maharashtra, the participants were willing to switch to cups as it was economically feasible and also comfortable to use.[16] Another study on menstrual hygiene of adolescent girls in India discussed that cups may be economically advantageous to use, but its low usage may be attributed to concerns about virginity and breaking the hymen.[17] In a study conducted in Nepal, the use of vaginal MCs for menstrual hygiene management among schoolgirls showed feasible and acceptable, as it involves practical, economic, and environmental advantages. Nevertheless, the scale-up of MCs will require resolving described concerns and discomforts and fostering peer and family support.[18] The risk of urogenital diseases is much higher in Indian women due to certain menstrual hygiene practices such as reusing the menstrual cloth, as was emphasized.[19] The effect of menstrual hygiene on school going girls was conducted among 751 students among which, 644 were followed-up for a median of 10.9 months. The finding highlighted that the use of MCs was associated with lower levels of bacterial infections according to a study conducted in rural Western Kenya[20] These studies have shown a potential option of these cups in reproductive women. Perhaps there is paucity of data on the knowledge and awareness of MC among reproductive women in India.

METHODOLOGY

A cross-sectional and observational study was conducted among the females of reproductive age, between October 2022 and December 2022. A questionnaire was prepared using Google Forms and was shared through various social media platforms. The study was approved by the Institutional Ethics Committee, Apollo Hospitals, Chennai. Females with reproductive stage and who understand the contents of the questionnaire and willing to participate in the study were included in the study. The questionnaire consists of the following sections: the first section includes demographic and anthropometric details which included age, marital status, educational qualification, occupation, and monthly expenditure toward sanitary products were recorded accordingly. The second section includes the questions related to perception, knowledge, and awareness related to MC. The baseline characteristics of the participants were presented as frequency and percentages. The data were analyzed using SPSS version 22.0 (IBM). $P \leq 0.05$ was considered statistically significant for all analyses.

RESULTS

A total of 340 participants were responded, among with 325 were included in the study. Table 1 shows the demographic profile of the respondent. In the present study, majority of the responders were aged between 18 and 25 (38.15%), followed by 26–35 years (34.76%). Majority of the responders belongs to urban area (41.23%). Occupation of the women shows that 32% of the respondents are employed, 25.84% students, 22.46% unemployed, and 15.07% are home makers. Expenditure toward the sanitary products ranged between 100 and 300 Rs. per month (44.9%). The source of information about the MC for the responders was friends (68.92%), followed by family (23.07%), media (4.30%), and medical personal (3.69%). In terms of usage of sanitary pads, majority of the responders used sanitary pads (79.38%), followed by cloths (12.38%). Of the study population, only 3.69% actually use MC.

Table 2 shows the knowledge on MC among age groups. Majority of the participants responded that the MC is a safe device (54.76%), it can be used in virgins (60.61%), aware about the mechanism of action (58.59%), aware about the emptying time of the cup (6–12 h) (48.30%), sterilization of the cup (60.61%), and used during postpartum (57.84%). There is significant difference between the age group less than 35 and <35 in knowledge on MC ($P = 0.001$).

Figure 1 depicts the attitude toward MC. Majority of the responders agreed that the MC is environmentally friendly (88.3%), easy to adapt (76.61%), would be comfortable (73.84%), hygiene (72.3%), easy to clean (70.46%), easy

to wear (68.30%), and easy to remove (63.07%). Perhaps majority of the individuals feels that it is not cheaper (68.3%). There is a significant difference between the responders aged <35 years and aged above 35 years ($P = 0.001$).

Figure 2 depicts the technical concerns about the MC. Majority of the responders are concerned for leakage (57.84%), inserting in vagina (57.23%), and fear of allergies (57.84%). Perhaps among the responders who were using MC (3.69%), they were not concerned about the leakage, vaginal insertion, or allergies. About 63.07% of the responders would like to use MC if it is made available. The reason for non-preference of MC were affordability (88.92%), followed by accessibility (60.92%), social taboo (52%), and limited knowledge (45.23%) [Table 3].

Table 1: Demographics parameters of the study participants

S. No.	Variable	*n* (%)
1	Age	
	18–25	124 (38.15)
	26–35	113 (34.76)
	36–45	88 (27.07)
2	Place of residence	
	Urban	134 (41.23)
	Semi urban	111 (34.15)
	Rural	80 (24.61)
3	Occupation	
	Student	84 (25.84)
	Employed	104 (32)
	Unemployed	73 (22.46)
	Homemaker	49 (15.07)
	Business	15 (4.6)
4	Monthly expenditure toward sanitary products (Rs)	
	0–100	39 (12)
	100–300	146 (44.9)
	300–500	97 (29.84)
	>500	43 (13.2)
5	Sanitary products currently used	
	Sanitary pads	258 (79.38)
	Tampons	5 (1.53)
	Menstrual Cups	12 (3.69)
	Cloths	50 (15.38)
6	Source of information	
	Family	75 (23.07)
	Friends	224 (68.92)
	Media	14 (4.30)
	Medical personnel	12 (3.69)
7	Menstrual cup made up of	
	Silicon	91 (28)
	Rubber	65 (20)
	Latex	114 (30.07)
	All the above	55 (16.92)

DISCUSSION

The present study highlighted that the social media is an effective information source (68.92%), with the majority of participants getting their information through social media, whereas in previous studies, only about 36.7% were reported to know about the MC from social media.[21,22] In the same survey, the respondents reported that the durability, low economic costs, eco-friendliness, and reusable nature of the MC were the main reason behind its popularity. In the present study maximum of the study, participants were in the 18–25 years of age group. Maximum number of earlier studies assessed the level of knowledge of MC usage among the adolescent girls.[3] Perhaps the present study focused on the reproductive group. A recent study finding suggested that a total of 82% were aware about the MC, perhaps only 2.6% have used.[2] Similarly, in the present study, only 3.6% were used MC. To maintain sanitary hygiene on menstrual days, the majority of responders utilized sanitary pads either alone or in combination with cloth, tampons, and MCs. According to research conducted in India, most girls who attend school and adults also use sanitary napkins.[23-25] This may be because napkins are offered at primary health-care centers for free or because menstruation cups are less popular among women of these ages than sanitary pads and cloth.[14,25]

In a meta-analysis, 70% of people from 13 studies indicated their readiness to continue using menstruation cups.[14] Although most of the participants in the present study were aware of MCs, most had never ever used one. Moreover, only 3.6% of women were found to have

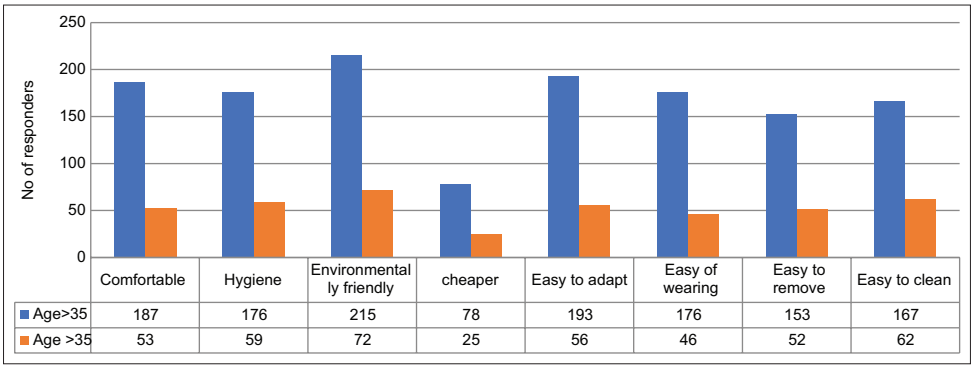

Figure 1: Attitude toward menstrual cup

Table 2: Knowledge on menstrual cup among age groups

S. No.	Variable	*n* (%) *n*=325	Age >35 years *n*=237 (%)	Age <35 years *n*=88 (%)
1	Menstrual cup is safe device			
	Yes	178 (54.76)	112 (47.25)	66 (75)*
	No	147 (45.23)	125 (52.74)	22 (25)*
2	Can it be used in virgins			
	Yes	197 (60.61)	145 (61.18)	52 (59.09)
	No	128 (39.38)	92 (38.81)	36 (40.9)
3	Awareness of mechanism of action			
	Yes	168 (51.69)	126 (53.16)	42 (47.72)*
	No	157 (48.3)	111 (46.83)	46 (52.27)*
4	Mechanism of action			
	Collection	98 (58.33)	78 (32.91)	20 (22.72)*
	Absorption	70 (41.66)	48 (38.09)	22 (52.38)*
5	Emptying time of cup			
	2 h	54 (16.61)	31 (24.6)	23 (54.76)*
	6–12 h	157 (48.3)	113 (47.67)	44 (50)
	Don't know	114 (35.07)	93 (39.24)	21 (23.86)*
6	Mode of sterilization of cup			
	Washing with water	87 (26.76)	72 (30.37)	15 (17.04)*
	Boiling	114 (35.07)	82 (34.59)	32 (36.36)
	Using microwave	74 (22.76)	42 (17.72)	32 (36.36)*
	All the above	50 (15.38)	41 (17.29)	9 (10.27)*
7	Sterilization of cup			
	Yes	197 (60.61)	160 (67.51)	37 (42.4)*
	No	128 (39.38)	77 (32.48)	51 (57.95)*
8	Can it be used in postpartum			
	Yes	188 (57.84)	162 (68.35)	26 (29.54)*
	No	137 (42.15)	75 (31.64)	62 (70.45)*
9	Can it be used while swimming			
	Yes	186 (57.23)	151 (63.71)	35 (39.77)*
	No	139 (42.76)	86 (36.28)	53 (60.22)*
10	Can it be used while bathing			
	Yes	247 (76)	195 (82.27)	52 (59.09)*
	No	78 (24)	42 (17.72)	36 (40.9)*
11	Can it be used while sleeping			
	Yes	186 (57.23)	147 (62.02)	39 (44.31)*
	No	139 (42.76)	90 (37.97)	49 (55.68)*

*$P \leq 0.001$

Table 3: Reason for non- preference

S. No.	Reason for non-preference	*n* (%)
1	Accessibility	198 (60.92)
2	Social Taboo	172 (52.92)
3	Limited knowledge	147 (45.23)
4	Affordability	289 (88.92)

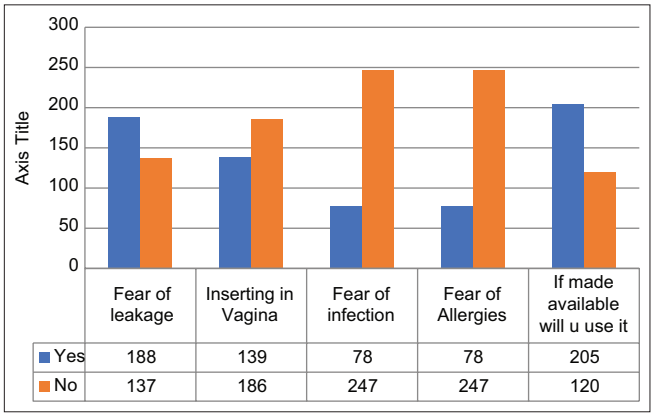

Figure 2: Technical concerns about menstrual cup

used a MC. Therefore, additional analysis of cleanliness and MC leaking was outside the purview of the study. Similar research in Gujarat revealed that adults between the ages of 20 and 50 preferred using MCs because they were simpler to insert and remove, more comfortable, less smelly, and had less side effects including rashes and dryness.[24] Even though the study participants were well aware of the practice and hygiene of the MC, the assessment of acceptability of the cup based on the questionnaire should be further investigated by prospective observational studies.

Although menstruation cups have many advantages over other products used for the period management, it has not been widely adopted due to poor knowledge and promotion. The urgent requirement is to raise awareness of the product and make it available in all pharmacies and super markets. Healthcare workers can be involved

in creating awareness and also to assist the use of MC to improve the hygiene. It is simple to raise the level of health with the assistance of health increase menstrual hygiene knowledge and support the use of MCs to enhance it at a reduced cost.

CONCLUSION

In the present study, the MC knowledge and attitudes, and behaviors of reproductive women were carefully examined. This study concluded that even though many of the participants were aware of the MC's use, it has not yet been widely accepted or used. There is a significant disconnect between women's understanding about and desire to use menstruation cups. The use of these cups can be implemented because they are, environmentally friendly, and reusable, especially in rural areas of India. This survey also revealed that the majority of participants are willing to utilize the MC if one is made available. There was a lack of awareness on the advantages of the MC over sanitary pads. In developing countries like India, there is an inadequate solid waste management, thus there is a need to increase the use of MCs. Youth should be addressed, since they are more receptive to the idea of eco-friendly products, to increase the adoption rate of menstruation cups. MCs can last up to 10 years and produce less waste when compared to other traditional methods. Thus, it is economically feasible and cost effective. Government must implement awareness campaigns in rural areas and continue to disseminate awareness among all socioeconomic levels, for "pad free country."

The knowledge, attitude, and acceptance for the usage of menstruation cups among the educated classes are well acknowledged despite the limitations of this study. Despite the fact that most individuals are aware of MC, many myths are prevalent. Between willingness to use and actual use, there is a significant gap. The usage of menstruation cups among Indians, particularly in rural areas where access to basic resources is prohibited, can be implemented thanks to the fact that they are reusable, require less water to clean, and also promote cleanliness. Therefore, managing menstrual hygiene is a growingly significant (but sometimes ignored) topic that is closely linked to girls' empowerment, education, and societal growth. Therefore, promoting the use of cups and counseling initiatives that emphasize excellent sanitary hygiene practices for females by government agencies through health workers should be prioritized as the main objective. In the long run, these programs may have an effect on a larger number of women who are not now participating. To improve the KAP, targeted health education programs are required.

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Original Article

A Cross-sectional Study on Correlation between Serum Lipid Profile and Microalbuminuria among Normotensive Diabetic Patients Attending a Tertiary Care Hospital, Bangalore

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Abstract

Background: Diabetes mellitus is considered to be the most serious risk factor for cardiovascular disease. Studies on diabetic populations have indicated that patients with albuminuria are at particularly high risk of cardiovascular morbidity and mortality. Individuals with diabetes mellitus may have several form of dyslipidemia. Some studies have shown that hyperlipidemia contributes to both macrovascular changes and to nephropathy. The most common pattern of dyslipidemia is hypertriglyceridemia and reduced high-density lipoprotein (HDL) cholesterol levels. The objective of present study is to study the relationship between dyslipidemia and albuminuria in diabetic subjects attending KIMS OPD.

Methods: In the present study, 100 patients with diabetes mellitus, 50 patients with microalbuminuria in Group I, and 50 patients with normoalbuminuria in Group II were included and the relationship between dyslipidemia and microalbuminuria was studied.

Results: Majority of the study participants belonged to the age group 61–70 years (33%) of age. The mean age of the study participants was found to be 57.26 ± 12.35. Overall, the mean lipid profile parameters were higher among Group I (with microalbuminuria) when compared with Group II (normoalbuminuria). The association was found to be statistically significant between the total cholesterol (TC), triglycerides (TG), HDL, and low-density lipoprotein (LDL) and the two groups of study participants. When TC, TG, HDL, and LDL values of the study participants were correlated with albuminuria values, positive correlation was found between the lipid profile parameters and the albuminuria levels and the correlation was found to be statistically significant.

Conclusion: To improve the prognosis and the quality of life in the diabetic patients even further, the treatment and care of patients must deal with all aspects of the disease, and thus, prevention and treatment of micro and macrovascular complications become vital. Early detection of high-risk patients, even before development of microalbuminuria, is of substantial importance to target early intervention at complication of diabetes.

Key words: Diabetes mellitus, Dyslipidemia, Hyperglycemia, Microalbuminuria

INTRODUCTION

"Diabetes mellitus is a syndrome with disordered metabolism and inappropriate hyperglycemia due to either a deficiency of insulin secretion or due to insulin resistance and increased insulin secretion to compensate or due to a combination of the two."[1] In recent years, diabetes mellitus has been found to be the most serious risk factor for cardiovascular disease identified at the individual level.[2] Increased urinary albumin excretion rate (UAER), even in the early microalbuminuric range, is associated with progressive renal failure and increased cardiovascular morbidity and mortality in diabetic and non-diabetic patients.[3-5] Although lipid metabolism has been extensively investigated in diabetes, little information is available concerning the lipid abnormalities associated with increased UAER.

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Objective of the Study

The objectives of this study were as follows:

- To study the relationship between dyslipidemia and albuminuria in patients with diabetes mellitus.

METHODS

Study Design

This study was cross-sectional study.

Study Duration

This study was 24 months (September 2019–August 2021).

Study Area

This study was Kempegowda Institute of Medical Science, Bangaluru.

Study Participants

This study was type II diabetes mellitus above 35 years attending the Medicine OPD/IPD of KIMS Hospital, Bangaluru.

Inclusion Criteria

The following criteria were included in the study:

1. Type II diabetes mellitus patients above 35 years
2. Type II diabetic patients with normoalbuminuria
3. Type II diabetic patients with microalbuminuria.

Exclusion Criteria

The following criteria were excluded from the study:

1. Pregnant patients
2. History of non-diabetic renal disease
3. Patients on lipid-lowering agents.

Conditions with transient increase in albuminuria such as urinary tract infections, acute febrile illnesses, burns, and marked hypertension.

Estimation of Sample Size

On the basis of statistics obtained from Department of Medicine, M.V.J. Medical College and Research Hospital, an average of five cases per month fitting the criteria of the study with study duration of 24 months, we can expect to have $n = 120$. Based on this population size, using

Table 1: Distribution of the study participants according to their age group

Age	Frequency *n*	Percentage
31–40 years	13	13
41–50 years	23	23
51–60 years	21	21
61–70 years	33	33
71–80 years	6	6
81–90 years	4	4
Mean±SD	57.26±12.35	

Table 2: Blood pressure among the two groups of study participants

Groups of study participants	SBP	DBP
Group 1		
Mean	120.20	78.60
SD	14.497	9.691
Group 2		
Mean	116.40	76.00
SD	10.053	6.999
Total		
Mean	118.30	77.30
SD	12.557	8.511

SBP: Systolic blood pressure, DBP: diastolic blood pressure

Table 3: Laboratory parameters among the two groups of study participants

Laboratory parameters	Mean	SD	95% CI for mean		*P*-value
			Lower bound	Upper bound	
Albuminuria value					
Group 1	73.19	825.60	65.920	80.476	0.000
Group 2	11.220	4.55	9.926	12.514	
Total	42.20	936.12	35.041	49.377	
Total cholesterol					
Group 1	228.80	54.89	213.20	244.40	0.000
Group 2	109.86	31.50	100.91	118.81	
Total	169.33	74.53	154.54	184.12	
Triglycerides					
Group 1	210.32	81.47	187.16	233.48	0.000
Group 2	92.22	36.73	81.78	102.66	
Total	151.27	86.46	134.11	168.43	
HDL					
Group 1	41.44	016.45	36.763	46.117	0.004
Group 2	34.106	5.67	32.494	35.718	
Total	37.77	312.78	35.236	40.310	
LDL					
Group 1	144.10	34.23	134.37	153.83	0.000
Group 2	82.16	32.71	72.86	91.46	
Total	113.13	45.59	104.08	122.18	

**t*-test, HDL: High-density lipoprotein, LDL: Low-density lipoprotein

Table 4: Correlation between lipid profile parameters and albuminuria values

Lipid profile parameters	Albuminuria value
Total cholesterol	
Pearson correlation	0.814*
Sig. (two-tailed)	0.000
Triglycerides	
Pearson correlation	0.740*
Sig. (two-tailed)	0.000
HDL	
Pearson correlation	0.160
Sig. (two-tailed)	0.113
LDL	
Pearson correlation	0.641*
Sig. (two-tailed)	0.000

*Strong positive correlation, HDL: High-density lipoprotein, LDL: Low-density lipoprotein

YAMANE equation, for a known population size, sample size (n) equal to

$$n = N/1+Ne2$$

n = sample size
n = population size
e= margin of error (for 95% of confidence level, margin error =0.05)
n = 120/1+120*0.05*0.05 = 120/1.3 = 92.30

Therefore after approximating, the sample size of the study participants was fixed at 100.

The study participants were divided into group of 2, with 50 study participants per group.

- Group I: Study participants with microalbuminuria (50 patients)
- Group II: Study participants with normoalbuminuria (50 subjects).

RESULTS

Majority of the study participants belonged to the age group 61–70 years (33%) of age. As seen from Table 1 , the mean age of the study participants was found to be 57.26 ± 12.35.

As seen in the above Table 2, the mean and standard deviation of the blood pressure among the two groups of study participants are comparable to each other

The above table 3, shows the mean and standard deviation of lipid profile parameters of the two groups of study participants. The association was found to be statistically significant between total cholesterol (TC), triglycerides (TG), high-density lipoprotein (HDL), and low-density lipoprotein (LDL) and the two groups of study participants.

The above figure shows the mean plots of laboratory parameters among the study participants. Overall, the mean laboratory parameters pertaining to the study were higher among Group I (with microalbuminuria).

When TC, TG, HDL, and LDL values of the study participants were correlated with albuminuria values as seen from above table 4, a positive correlation was found between the lipid profile parameters and the albuminuria levels, and the correlation was found to be statistically significant between TC, TG's, LDL and urine albumin levels [Figure 1].

As seen from Figure 2, as the urine albumin levels increases, TG and TC values also increase.

As seen from Figure 3, as the urine albumin levels increases, LDL levels also increase.

DISCUSSION

The present study, 100 patients with diabetes mellitus, 50 patients with microalbuminuria in Group I, and 50 patients with normoalbuminuria in Group II were included and the relationship between dyslipidemia and albuminuria was studied.

In the present study, majority of the study participants belonged to the age group 61–70 years (33%) of age.

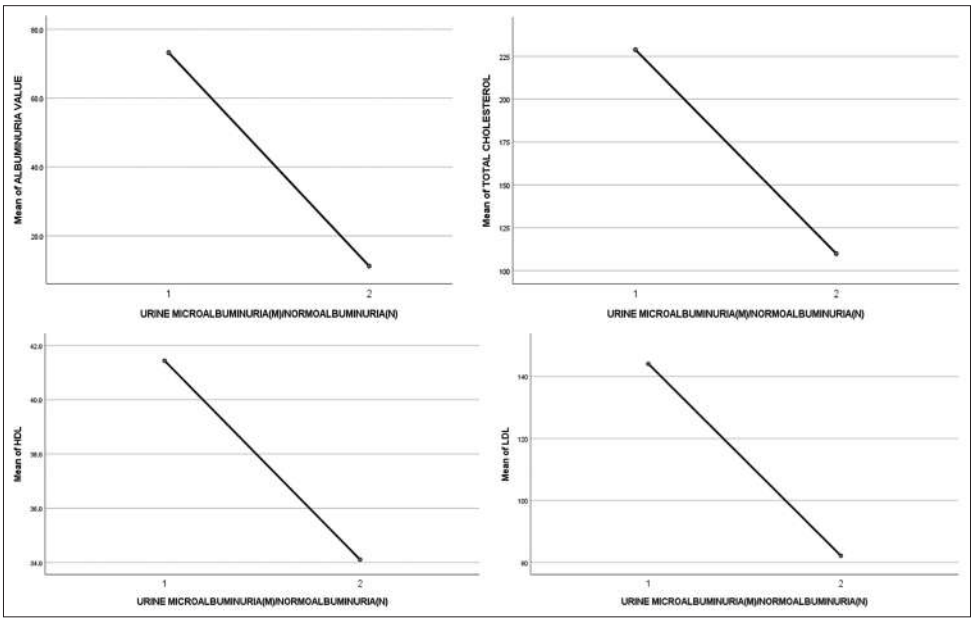

Figure 1: Mean plots of the laboratory parameters among the two group of study participants

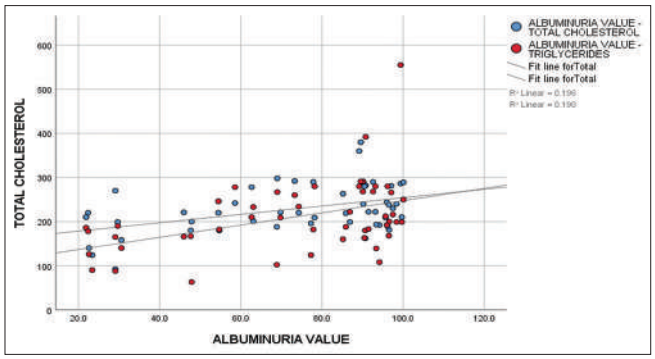

Figure 2: Correlation between albuminuria and total cholesterol, triglycerides

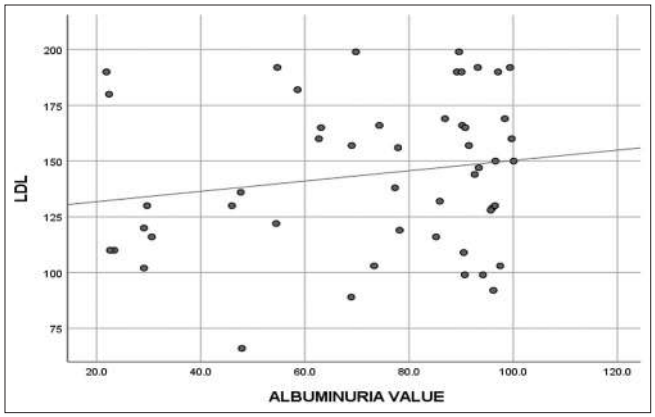

Figure 3: Correlation between albuminuria and low-density lipoprotein

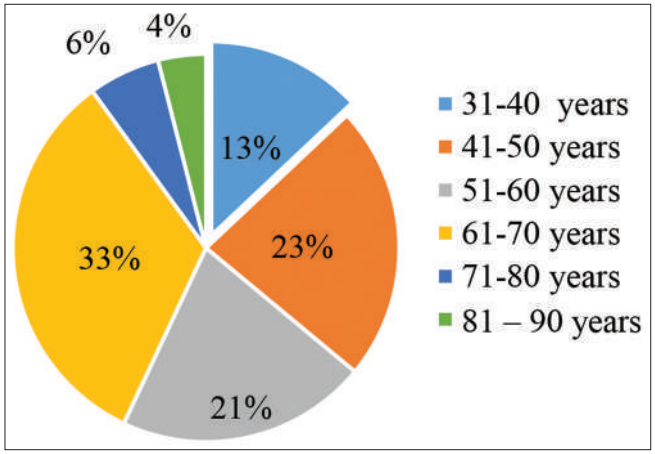

Figure 4: Distribution of the study participants according to their age group

The mean age of the study participants was found to be 57.26 ± 12.35. In a study done by Basu and Jhala,[6] the mean age of the study participants was found to be 57.36 ± 4.08, which is similar to the findings of the present study [Figure 4].

In the present study, the mean lipid profile parameters were higher among Group I (with microalbuminuria) when compared with Group II (normoalbuminuria). The association was found to be statistically significant between the TC, TG, HDL, and LDL and the two groups of study participants. In a study done by Basu and Jhala,[6] the mean lipid profile parameters were higher among study participants with microalbuminuria when compared with study participants with normoalbuminuria, which is similar to the findings of the present study. They also found that the serum cholesterol and triglyceride levels were found significantly higher in patients with albuminuria than without it, ($P < 0.05$) showing that lipids may have a role in albuminuria in diabetic patients. In a study done by Tseng,[7] the albuminuric group was characterized by significantly higher levels of TC, TG, and LDL cholesterol. This is comparable with the findings of the present study.

In the present study, when TC, TG, HDL, and LDL values of the study participants were correlated with albuminuria values, positive correlation was found between the lipid profile parameters and the albuminuria levels, and the correlation was found to be statistically significant between TC, TG's, LDL, and urine albumin levels. In a study done by Vannini *et al*.,[8] no correlation between lipid parameters and amount of albuminuria was observed, which is in contrast with the findings of the present study. In a study done by Thomas *et al*.,[9] they found that dyslipidemia contributes to the progression of microvascular disease in diabetes. However, different lipid variables may be important at different stages of nephropathy.

CONCLUSION

The main risk factors for development, progression, and remission of microvascular disease in diabetic are much alike and closely interrelated. To improve the prognosis and the quality of life in the diabetic patients even further, the treatment and care of patients must deal with all aspects of the disease, and thus, prevention and treatment of micro- and macrovascular complications become vital. Early detection of high-risk patients, even before development of microalbuminuria, is of substantial importance to target early intervention at complication of diabetes.

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Original Article

Comparison Of Predictability of Moyers and Tanaka Johnson Mixed Dentition Analyses in Kottayam–Kerala Population

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Abstract

Introduction: Mixed dentition is a transition period of occlusion that has both primary and permanent teeth, usually lasts from 6 to 12 years, and is associated with maximum orthodontic problems due to the inadequacy of space for erupting permanent teeth. An early assessment of available space may permit early intervention or minimize the developing malocclusion.

Aims: The aims of this study were to evaluate the applicability of the Tanaka and Johnston (1974) and Moyers (1988) mixed dentition analyses in predicting the size of permanent canines and premolars in children of Kottayam population.

Methods: Cast models of 100 (50 females and 50 males) children aged between 12 and 16 years of age were included in the sample. Mesiodistal (m-d) widths of all teeth from left to right first molars were measured and compared with the predicted values derived from Tanaka and Johnston and Moyers methods.

Results: There was significant bilateral symmetry and sexual dimorphism in teeth sizes seen in both the sexes. Sum of the m-d diameter of permanent mandibular incisors can be used reliably to predict the sum of m-d diameters of unerupted canines and premolars.

Conclusion: Moyers prediction tables closer to 75% probability level Tanaka and Johnston's method cannot accurately predict the m-d width of unerupted canine and premolars. Both these methods underestimate the values. A new regression equation that better defines the mesiodistal width of canines and premolar is required for the children of Kottayam population and it is derived.

Key words: Kottayam, Moyer's analysis, Regression equation, Tanaka Johnston analysis

INTRODUCTION

The period of mixed dentition is a critical period for the prevention or interception of any developing malocclusion. Dental crowding is one of the most frequent dental problems in the general population. It is described as the discrepancy between tooth size and arch perimeter. Early diagnosis and successful treatment of dentoalveolar discrepancies can help in achieving the goals of occlusal harmony, function, and dental facial esthetics. In the transition (mixed) dentition, it is possible to accurately determine whether combined mesial-distal tooth size will be balanced with alveolar arch size in later life. This process of determination is called mixed dentition space analysis. The method of mixed dentition analysis predicts the mesiodistal width of permanent unerupted canines and premolars. It is a diagnostic tool that allows to quantify crowding and to predict dentoalveolar discrepancy by identifying the available and necessary space for teeth not yet erupted.

There have been various methods developed for space analysis and prediction of the sizes of unerupted teeth. The three basic approaches of predicting mesiodistal

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width of the permanent canines and premolars are direct measurements from the radiographs, correlation-statistical methods, and combination of radiographs and correlation-statistical methods. The prediction methods of Moyers and the Tanaka-Johnston mixed dentition space analysis have been widely adopted and are most commonly used in clinical practices. Moyers mixed dentition analysis is a non-radiographic method which uses mesiodistal width of four permanent lower incisors and a prediction table for unerupted canines and premolars, with percentiles ranging from 50 to 95 for American children.[1] Percentile 75 is recommended when applying the analysis in different populations. On the other hand, the Tanaka-Johnston analysis also uses mesiodistal width of four permanent lower incisors to develop regression equations for predicting the sizes of the unerupted canines and premolars.[2]

Moyers analysis was developed from data obtained from North American children, whereas Tanaka and Johnston equations were assembled on the basis of a sample of individuals of European descent. Evidence of racial tooth size variability, however, suggests that the prediction techniques based on a single racial sample may not be considered universal. Hence, it is important to evaluate the applicability of the Moyers and Tanaka-Johnston methods of mixed dentition analysis for various populations. Hence, the present study was carried out to determine the applicability of Moyers and Tanaka-Johnston mixed dentition analysis methods of prediction of width of unerupted permanent canines and premolars in Kottayam, Kerala population.

MATERIALS AND METHODS

The study sample consisting of 100 children (50 males and 50 females) within the age group of 12–16 years having full complement of erupted canine and premolars in both the arches from various areas of Kottayam district presenting to the outpatient department of Government Dental College, Kottayam. Details of procedure were thoroughly explained to parents and informed consent was obtained before study. Alginate impressions of both the maxillary and mandibular arches were made. The impressions were poured immediately in dental stone to prevent dimensional changes. The measurements of teeth on dental casts were done using a calibrated digital caliper with an accuracy of 0.01 mm. The greatest mesiodistal dimensions of the right and left canine and premolars of both maxillary and mandibular arches were measured separately and recorded (measured values). Sum of the mesiodistal width of four mandibular incisors were recorded to obtain the space for the eruption of canine and premolars for both the arches using Moyer's and Tanaka Johnston analysis (predicted value). All measurements were carried out twice and the mean of the two values were considered. Measured values were compared with the predicted values obtained by Moyers and Tanaka-Johnston mixed dentition analysis methods.

Inclusion Criteria

The following criteria were included in the study:

- The subjects were of Kottayam district for at least 1 year
- The subjects were in the age group of 12–16 years
- The teeth were free of proximal restorations, fractures, proximal caries, hypoplasia, or any anomalies of the teeth
- No developmentally missing or supernumerary teeth were present
- Subjects with severe crowding and who had previous orthodontic treatment were excluded.

Moyers Method[1](1988)

Predicted values of Moyers mixed dentition analysis are obtained using the sum of mesiodistal width of four permanent lower incisors and a prediction table for non-erupted canines and premolars, with percentiles ranging from 50 to 95 for American children. Percentile 75 is recommended when applying the analysis in different populations. The predicted values were compared with the measured values.

Tanaka-Johnston Method[2] (1974)

According to these equations, the sum of the mesiodistal width of four mandibular incisors is used to predict the mesiodistal width of unerupted permanent canines and premolars as follows:

For maxillary arch:

$Y = 11.0 + 0.5 (X)$

For mandibular arch:

$Y = 10.5 + 0.5 (X)$

Where,

Y = the predicted value of the sum of the mesiodistal width of the unerupted canines and premolars on either the right or left side.

X = the sum of the mesiodistal width of the four mandibular incisors.

The difference between the measured values of sum of mesiodistal width of the canine and premolars and the predicted values according to Moyers and Tanaka-Johnston methods were tested for significance using students unpaired *t*-test and compared using Pearson correlation.

RESULTS

Comparison of combined mesiodistal width of canine and premolars in maxillary and mandibular right and

left quadrants with the measured value of maxillary and mandibular right and left quadrants, respectively, was found to be statistically insignificant with $P = 0.754$ (>0.05) and 0.657 (>0.05) [Table 1].

Correlation of Moyers analysis in Maxillary right and left quadrants shows difference in values of mesiodistal width of canine and premolars obtained by direct measuring and that obtained from Moyers analysis in maxillary right and left quadrants, respectively, which were found to be statistically significant ($P < 0.05$) [Table 2].

Correlation of Moyers analysis in mandibular right and left quadrants shows difference in values of mesiodistal width of canine and premolars obtained by direct measuring and that obtained from Moyers analysis in mandibular right and left quadrants, respectively, which were found to be statistically significant ($P < 0.05$) [Table 3].

Correlation of Tanaka Johnson analysis in maxillary right and left quadrant shows difference in values of mesiodistal width of canine and premolars obtained by direct measuring and that obtained from Tanaka Johnson analysis in maxillary right and left quadrant, respectively, which is statistically significant ($P < 0.05$) and having a correlation only 0.813 [Table 4].

Correlation of Tanaka Johnson analysis in mandibular right and left quadrant shows difference in values of mesiodistal width of canine and premolars obtained by direct measuring and that obtained from Tanaka Johnson analysis in mandibular right and left quadrant which is statistically significant with $P < 0.05$ [Table 5].

Regressive Equations for Males and Females

Both Moyer's and Tanaka Johnston mixed dentition analysis are having a low correlation value among the population under our study. Hence, a new regression equation with a high correlation value was derived. Linear regression is used to predict the width of unerupted canines and premolars using the width of anterior teeth in Kottayam population.

Regressive equations for maxilla of males [Table 6 and Figure 1].

Regressive equations for mandible of males [Table 7 and Figure 2].

Regressive equations for maxilla of females [Table 8 and Figure 3].

Regressive equations for mandible of females [Table 9 and Figure 4].

Table 1: Comparison of combined mesiodistal width of canines and premolars on the right and left quadrants of maxillary and mandibular arch

Quadrant	Side	*n*	Mean±SD	*P*
Maxillary	Right	100	22.75±1.28	0.754
	Left	100	22.69±1.24	
Mandibular	Right	100	21.55±1.52	0.657
	Left	100	21.64±1.47	

SD: Standard deviation

Table 2: Correlation of Moyers analysis in maxillary right and left quadrants with the measured value

Quadrant and side	*n*	*P*	Pearson correlation
Maxillary right			
Measured value	100	0.000	0.706
Moyers analysis	100		
Maxillary left			
Measured value	100	0.000	0.723
Moyers analysis	100		

Table 3: Correlation of Moyers analysis in mandibular right and left quadrants with the measured value

Quadrant and side	*n*	*P*	Pearson correlation
Mandibular right			
Measured value	100	0.000	0.576
Moyers analysis	100		
Mandibular left			
Measured value	100	0.000	0.710
Moyers analysis	100		

Table 4: Correlation of Tanaka Johnson analysis in maxillary right and left quadrants with the measured value

Quadrant and side	*n*	*P*	Pearson correlation
Maxillary right			
Measured value	100	0.000	0.813
Tanaka Johnson analysis	100		
Maxillary left			
Measured value	100	0.000	0.813
Tanaka Johnson analysis	100		

Table 5: Correlation of Tanaka Johnson analysis in mandibular right and left quadrants with the measured value

Quadrant and side	*n*	*P*	Pearson correlation
Mandibular right			
Measured value	100	0.000	0.580
Tanaka Johnson analysis	100		
Mandibular left			
Measured value	100	0.000	0.722
Tanaka Johnson analysis	100		

DISCUSSION

Moyers mixed dentition analysis uses sum of mesiodistal width of four permanent lower incisors and a prediction table for non-erupted canines and premolars, with percentiles ranging from 50 to 95 for American children. Percentile 75 is recommended when applying the analysis in different populations. On the other hand, the Tanaka-Johnston mixed dentition analysis uses the sum of mesiodistal width of the mandibular central and lateral incisors to develop regression equations for predicting the sizes of the unerupted canines and premolars.

Moyers analysis was developed from data obtained from North American children, whereas Tanaka and Johnston equations were assembled on the basis of a sample of individuals of European descent. Evidence of racial tooth size variability however suggests that the prediction techniques based on a single racial sample may not be considered universal. Schirmer and Wiltshire,[3] Nourallah *et al*.,[4] and Bonetti *et al*.[5] evaluated the applicability of Tanaka and Johnston's and Moyers' methods for black South Africans, Syrians, and northern Italians, respectively. These studies confirmed statistically significant differences between the predicted and actual mesiodistal width of permanent canines and premolars using Moyers and Tanaka-Johnston mixed dentition analyses when applied to different racial groups. Hence, the present study was carried out to determine the applicability of above-mentioned mixed dentition methods of prediction of width of unerupted permanent canines and premolars in Kottayam district in Kerala population.

When the Tanaka-Johnston mixed dentition analysis method was applied on the Kottayam children sample, it was found that the Tanaka-Johnston equations also show deviation from actual measured value Tanaka Johnson equations also underestimated the estimated the actual values of sum of the mesiodistal width of the canine and premolars in both dental arches in total sample as well as in both sexes separately. There were statistically significant differences between the predicted values and their actual values. Similar results are also seen with studies conducted by Schirmer and Wiltshire[3] in 1997 and Jaroontham and Godfrey[6] These results are contrary to several studies conducted by Ramesh *et al*.[7] in Kodava population, Buwembo *et al*.[8] for Ugandan population and Grover *et al*. (2017)[9] for Lucknow population. They found that the Tanaka-Johnston prediction equations overestimated the actual values of the sum of canine and premolars. Underprediction has also been found with Tanaka-Johnston equations in other populations including Asian Americans by Lee-Chan *et al*.[10] and Hong Kong Chinese by Yuen *et al*.[11] Kaplan *et al*.[12] found that both Moyers and

Table 6: Regressive equations for maxilla of males

Coefficients					
Model 1	Unstandardized coefficients		Standardized coefficients β	*t*	Significant
	B	SE			
Constant	7.302	1.814		4.025	0.000
SOIs	0.666	0.076	0.784	8.745	0.000

SOIs: Sum of incisors, SE: Standard error

Table 7: Regressive equations for mandible of males

Coefficients					
Model 1	Unstandardized coefficients		Standardized coefficients β	*t*	Significant
	B	SE			
Constant	6.014	2.456		2.449	0.018
SOIs	0.679	0.103	0.689	6.589	0.000

SOIs: Sum of incisors, SE: Standard error

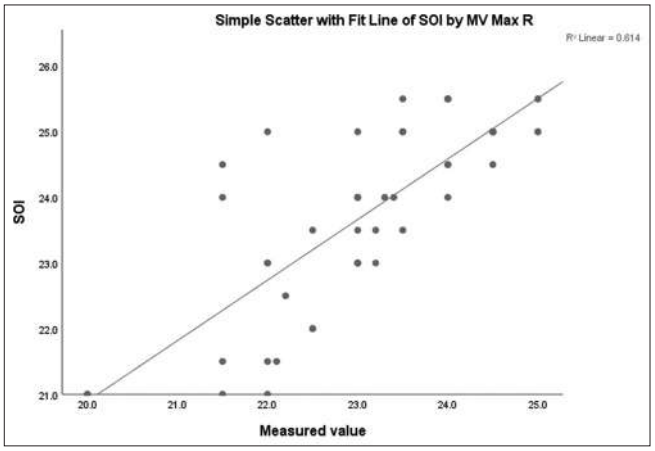

Figure 1: Sum of m-d width of canine plus premolar = 7.302+0.666 SOI

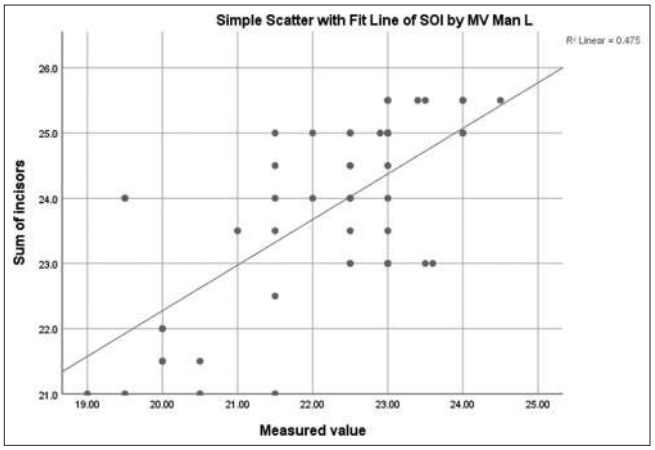

Figure 2: Sum of m-d width of canine plus premolar = 6.014+0.679 SOI

Tanaka-Johnston equations tend to overestimate the size of unerupted canines and premolar.

Table 8: Regressive equations for maxilla of females

Coefficients					
Model 1	Unstandardized coefficients		Standardized coefficients β	*t*	Significant
	B	SE			
Constant	6.612	1.679		3.937	0.000
SOIs	0.704	0.075	0.805	9.403	0.000

SOIs: Sum of incisors, SE: Standard error

Table 9: Regressive equations for mandible of females

Coefficients					
Model 1	Unstandardized coefficients		Standardized coefficients β	*t*	Significant
	B	SE			
Constant	6.854	2.305		2.974	0.005
SOIs	0.637	0.103	0.667	6.205	0.000

SOIs: Sum of incisors, SE: Standard error

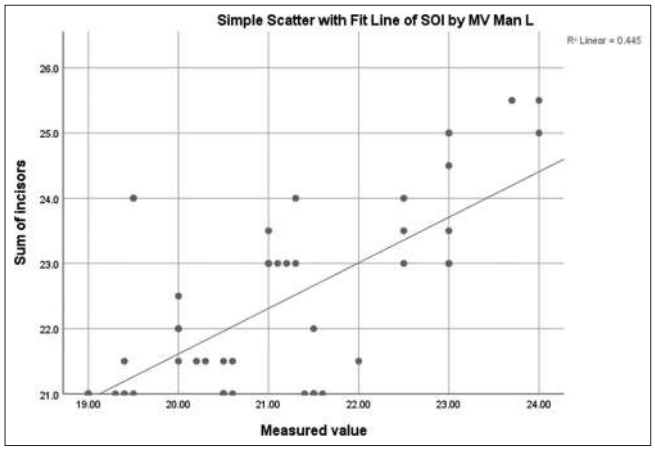

Figure 3: Sum of m-d width of canine plus premolar = 6.612+0.704 SOI

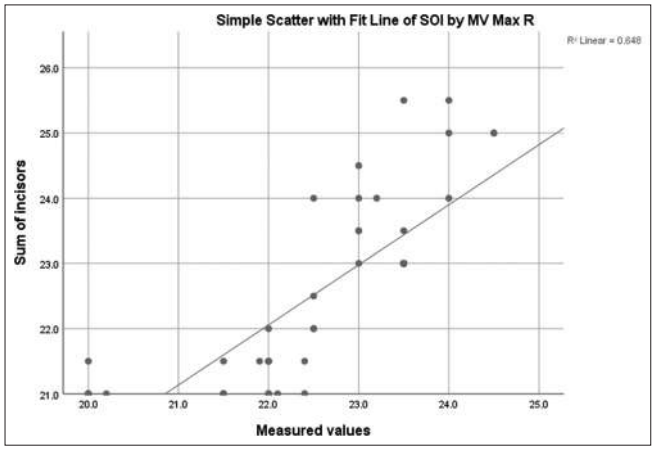

Figure 4: Sum of m-d width of canine plus premolar = 6.854+0.637SOI

Racial and gender specific-mixed dentition analyses require revision and validation once every generation due to changing trends in malocclusion and tooth size. Hence, we have derived four different equations for Kottayam population, two for males and two for females based on the sum of mandibular incisors as independent variable. The equations are given down as follows.

Equation for Male

- Maxillary quadrant: 7.302+0.666×
- Mandibular quadrant: 6.014+0.679×

Equation for Female

- Maxillary quadrant: 6.612+0.704×
- Mandibular quadrant: 6.854+0.637×

CONCLUSION

Moyers at 75% and Tanaka-Johnston mixed dentition analysis methods were not applicable for children of Kottayam population as both these methods underestimated the sum of the mesiodistal width of the permanent canine and premolars in both dental arches. Hence, we have derived four different equations for Kottayam population, two for males and two for females. New more accurate prediction equations which add sum of the mesiodistal width of the permanent canine and premolars in both arches for total sample as well as separately for male and female children have been formulated.

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Original Article

Knowledge of hypoglycemia and associated factors in patients with Type 2 diabetes mellitus: A tertiary care center based cross-sectional study from kerala

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Abstract

Context: Hypoglycemia is a life-threatening complication frequently encountered in patients with diabetes. Awareness of risk factors, symptoms, complications, and initial treatment will prevent occurrence of hypoglycemia. We identified a dearth of studies and a gap in knowledge on various aspects of hypoglycemia in Kerala.

Aim: This study was carried out to estimate the level of knowledge of hypoglycemia among Type 2 diabetes mellitus patients and to determine its association with sociodemographic factors, disease, and treatment modality.

Materials and Methods: A hospital-based cross-sectional study was carried out in the medicine OPD of a tertiary care center in Central Kerala. One hundred diabetic patients who consented to take part in the study were interviewed using a pre-validated questionnaire. The level of knowledge of hypoglycemia and its association with selected variables was analyzed.

Results: Among the 100 participants, 57% were females and majority (56%) had secondary education. Good knowledge about hypoglycemia was seen in only 46% of the subjects. A prior personal experience of hypoglycemia, treating doctors being the source of information, and duration of diabetes of more than 10 years were factors significantly associated with good knowledge.

Conclusion: Awareness of remedial measures of hypoglycemia is very good. However, knowledge of other important aspects such as symptoms, precipitating factors, preventive measures, and complications is alarmingly lacking even in an educated group of patients. Health education and reinforcement at every visit by health-care professionals is the need of the hour. Usage of social media and other innovative strategies to spread awareness post-pandemic needs to be considered.

Key words: Health education, Hypoglycemia, Knowledge, Social media, Type 2 diabetes mellitus

Key messages: Knowledge of important aspects of hypoglycemia such as symptoms, precipitating factors, preventive measures, and complications is alarmingly lacking even in an educated group of patients. Concerted efforts by health-care professionals using innovative strategies and social media to spread awareness post-pandemic is the need of the hour

INTRODUCTION

Hypoglycemia is a life-threatening complication occurring as a result of strict glycemic control in patients with Type 2 diabetes. It is characterized by the classic Whipple's triad of reduced plasma glucose, symptoms compatible with hypoglycemia, and rapid resolution of symptoms by correction of low glucose.[1] Strict glycemic control is advocated universally. However, randomized control trials such as VADT, ADVANCE, ACCORD, and DCCT have reported an increase in mortality and threefold increase in hypoglycemia in patients with intensive glycemic control regimens targeting aggressive HbA1c levels (<6.5%).[2] It leads to different adrenergic symptoms due to sympathetic nervous system activation and neuroglycopenic symptoms as a result of a decreased level of glucose in the brain.[3] These symptoms help people understand that their blood

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sugar is low. If left untreated, it can adversely affect workplace productivity, result in impairment in cognitive function, and is even associated with an increased risk of mortality.[4]

Awareness of risk factors of hypoglycemia, early recognition of hypoglycemic symptoms, self-monitoring of blood glucose (SMBG), and knowledge of correct initial treatment will minimize the risk of hypoglycemia and its complications. There is a paucity of studies and a gap in knowledge on various aspects of hypoglycemia in Kerala. Hence, this study was carried out to ascertain the level of knowledge of hypoglycemia and associated factors among Type 2 diabetes patients in central Kerala.

Objectives

The objectives of the study are as follows:

1) To estimate the level of knowledge of hypoglycemia among Type 2 diabetes mellitus patients
2) To determine the association of the knowledge of hypoglycemia with sociodemographic factors, disease and treatment profile of Type 2 diabetes mellitus patients.

MATERIALS AND METHODS

Study Design

This was a cross-sectional study.

Study Setting

The study was conducted in the Medicine outpatient department in a tertiary care hospital and medical college, Kerala.

Study Population

This study was carried out amongst Type 2 diabetes mellitus patients in central Kerala.

Operational Definitions

a) Knowledge – Refers to the state of being informed about the symptoms, risk factors, complications, preventive, and remedial measures of hypoglycemia
b) Type 2 diabetic patients – Patients already diagnosed with diabetes and have adopted life style modifications and/or taking medications which include oral hypoglycemic agents and/or insulin.

Inclusion Criteria

Patients with a diagnosis of Type 2 diabetes mellitus presenting to the outpatient department were included in the study.

Exclusion Criteria

The following patients were excluded from the study:

a) Patients with gestational or Type 1 diabetes mellitus
b) Patients with diabetes secondary to other systemic diseases.

Study Duration

The study duration was 3 months (January 2022–March 2022).

Sample Size

For sample size calculation, the formula $4\ pq/d^2$ was applied. Based on a previous study done by Shriraam *et al*., the proportion of patients with good knowledge on hypoglycemia was 66%.[5] The minimum sample size at 95% confidence limit and 15% allowable error was calculated to be 88. We included 100 patients in this study.

Data Collection

Diabetic patients who presented to the OPD were interviewed after obtaining an informed consent. Patients were recruited using convenient sampling. A pre-tested structured questionnaire was administered to the study participants by the primary investigator. Information on sociodemographic profile, disease history, and treatment profile of the study participants was collected. This was followed by questions testing the knowledge of patients about symptoms, risk factors, and complications of hypoglycemia. Few questions to assess their knowledge on preventive practices and immediate remedial measures that need to be adopted during an episode of hypoglycemia was also asked. The study included questions with a single correct option as the answer along with questions for which multiple options was considered as correct. Patients were asked to give a "yes," "no," or "I don't know" response. Participants who rightly answered the remedial measure along with at least three symptoms were considered as having "good knowledge" on hypoglycemia.

Statistical Analysis

The data were entered in "Microsoft Excel" software and analyzed using SPSS software. The categorical variables were summarized using frequency and percentage. To determine the association of knowledge of hypoglycemia with selective demographic and other variables, Chi-square test or Fischer's exact test was performed. $P < 0.05$ was considered as statistically significant.

Ethical Considerations

Institutional research and ethics committee approval was obtained before initiating the study. Confidentiality was ensured by maintaining participant anonymity when filling out the questionnaire.

RESULTS

The study included 100 patients who had Type 2 diabetes mellitus. The mean age of the study population was 63.98 ± 11.31 years. Among the participants, 57% of patients were females and majority (56%) had secondary education while

30% were graduates. Based on monthly income, population was almost evenly distributed with slight inclination toward income of Rs.10,000–20,000/- (34%). Majority of the participants were employed (53%), 36% unemployed or homemakers and the rest retired [Table 1].

Among the comorbidities along with diabetes, hypertension was found to be the most common disease (56%), followed by dyslipidemia (48%). Other diseases that were reported include coronary artery disease, chronic kidney disease, thyroid disorders, asthma etc., while 27% did not have any comorbidity [Figure 1].

Majority of the patients were diagnosed with diabetes for more than 10 years (43%), and 63% were taking oral hypoglycemic agents alone. Half the participants have a positive family history of diabetes and 63% reported to have had experienced hypoglycemia in the past while 28% had witnessed a family member go through hypoglycemia [Table 2].

The hypoglycemic alert value (70 mg/dL) was only known to 11%. The symptoms more commonly known to the participants were tremor (48%), sweating (38%) and confusion/disorientation (26%). Symptoms like pallor and seizure were known to a lesser extent as seen in Table 3. Three or more symptoms of hypoglycemia were known to 49 patients while 22 could not identify any symptom. The main precipitating factors identified by patients were skipping/missing meals (37%) and taking excess medication (32%). Remedial measures such as taking fast carbohydrates like glucose and sugar was known to most (79%) of the patients. Knowledge of complications of hypoglycemia was generally poor with heart problems being most commonly cited (27%). Around half the population were aware of and even practised measures to prevent hypoglycaemia such as taking medication on time (55%), keeping regular appointments (42%) and self-blood glucose monitoring (sbgm) (40%).Regarding source of information on hypoglycemia, 35% of the study subjects attributed it to their treating doctors. Health magazines and newspaper were the source for 27% and 23% heard about it from their friends and family members. However, 43% were not informed about hypoglycemia [Figure 2].Good knowledge about hypoglycemia was seen in 46% of the subjects [Figure 3].

Knowledge of hypoglycemia decreases with increase in age (among senior citizens), but the difference is not statistically significant. There is fair distribution of good knowledge among both sexes and no association was seen between gender and knowledge level. There is no statistical difference in knowledge of hypoglycemia with varying levels of education, monthly income, occupational status, or type of diabetic treatment.

A prior personal experience of hypoglycemia is a major determinant of having good knowledge of hypoglycemia ($P = 0.037$) with the difference being statistically significant. Duration of diabetes is another determining factor of

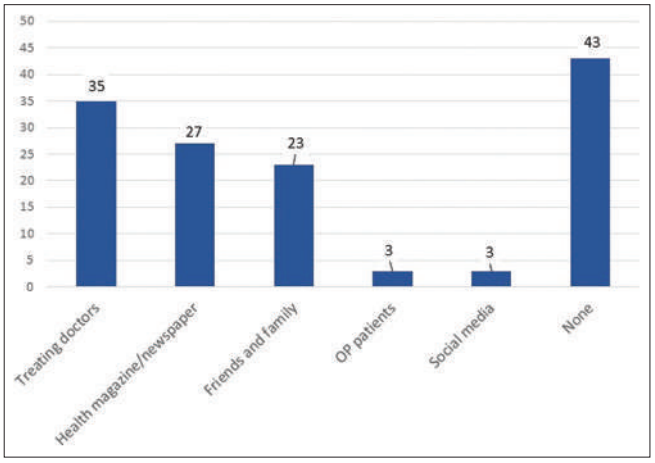

Figure 2: Source of information about hypoglycaemia

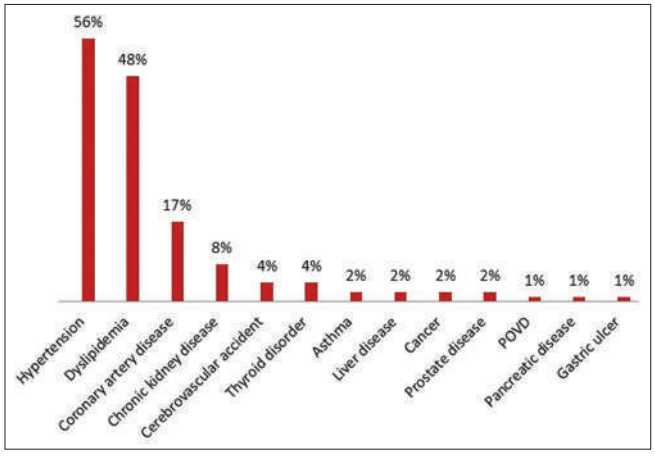

Figure 1: Prevalence of other co-morbidities along with diabetes

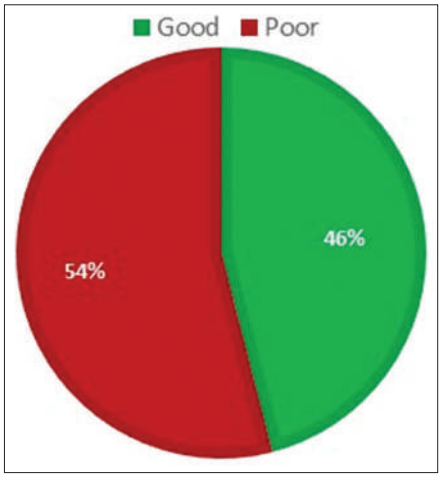

Figure 3: Knowledge about hypoglycaemia

knowledge of hypoglycemia ($P = 0.034$). A patient having diabetes for more than 10 years had significantly more knowledge on hypoglycemia than those with diabetes for < 10 years. Among the various sources of information, treating doctors significantly contributed to good knowledge about hypoglycemia ($P = 0.004$) [Table 4].

DISCUSSION

The study was conducted among 100 patients with Type 2 diabetes mellitus presenting to the medicine outpatient department of a tertiary care hospital in central Kerala. Even though a majority were from rural areas, 99% were literate. Overall, 46% of the participants had knowledge of at least three symptoms of hypoglycemia and its remedial measure (i.e., good knowledge).

Table 1: Sociodemographic factors of the study participants

Background characteristics	Frequency (%)
Sex	
Male	43
Female	57
Education	
No formal education	1
Primary (1–5)	13
Secondary (6–12)	56
Graduate or more	30
Monthly income	
<Rs. 10,000/-	24
Rs. 10,000–20,000/-	34
Rs. 20,000–30,000/-	20
>Rs. 30,000/-	22
Occupation	
Unemployed	36
Employed	53
Retired	11
Residence	
Urban	30
Rural	70

Table 2: Relevant background characteristics related to diabetes

Background characteristics	Frequency (%)
Type of diabetic treatment	
Lifestyle modifications only	4
Only oral hypoglycemic agents	61
Oral hypoglycemic agents and insulin	27
Only insulin	8
Duration of diabetes	
<5 years	36
6–10 years	21
>10 years	43
Family history of diabetes	50
Hypoglycemic experience	
Personal	63
Family	28

A prior personal experience of hypoglycemia and a greater duration of diabetes of more than 10 years, were factors significantly associated with a good knowledge of hypoglycemia as was also found in another study.[6]

Knowledge of hypoglycemia was found to improve with educational status; graduates faring better. It was less among senior citizens, probably attributable to a decline in cognition and memory. However, monthly income, residential or occupational status, and modality of diabetic treatment did not have any significant bearing on the same. However, another study done in South India reported a positive association of younger age, educational status, and treatment modality; that is, use of insulin along with oral hypoglycemic agents, with good knowledge of hypoglycemia.[5]

Among the symptoms of hypoglycemia, tremor and sweating were the most commonly known (48% and 38%, respectively), whereas neuroglycopenic symptoms such as seizure was known only to a handful (8%). This is similar to the frequency of occurrence of these symptoms during a hypoglycemic episode as observed in another study.[7] It is possible that this knowledge is related to the recollection of a prior personal experience of hypoglycemia which was seen in a majority (63%) of subjects in this study

Table 3: Knowledge of hypoglycemia among the participants

Knowledge about	Frequency (%)
Symptoms	
Tremor	48
Sweating	38
Confusion/disorientation	26
Hunger	24
Headache	16
Slurred speech	16
Pallor	13
Seizure	8
Precipitating factors	
Skipping/delaying meals	37
Excess medication	32
Excess consumption of alcohol	7
Vomiting	4
Remedial measure	
Take fast carbohydrate like sugar and glucose	79
Complications	
Heart problems	27
Loss of vision	12
Coma	10
Stroke like	10
Seizures	5
Preventive measures	
Timely medication	55
Regular appointment	42
SBGM	40
Refer doctor when infected	19
Refer doctor when going on a fast	11
Refer doctor when in rigorous exercise regimen	6

SBGM: Self blood glucose monitoring

and similar to another study held in Mysore.[6] However, around one-fifth (22%) were unable to identify even a single symptom. It is imperative that patients are aware of all possible presentations of hypoglycemia for the timely institution of preventive or remedial measures.

Skipping or delaying meals and excess medication intake were the common factors known to cause hypoglycemia. However, excessive alcohol consumption and vomiting were least known. Similar results were found in a study held in Rishikesh.[8]

Knowledge of complications of hypoglycemia was alarmingly poor. Only a tenth or less were aware of serious neurological complications such as stroke like symptoms, coma, and seizures. Multiple studies have reported similar unfamiliarity with complications.[1,4] Patients and their relatives must be able to recognize and promptly report to a hospital or clinic in the wake of such potentially life-threatening events.

Table 4: Association of good knowledge on hypoglycemia with certain background characteristics

Background characteristics	Good (%)	Poor (%)	*P*
Age			
Upto 50 years	8 (50)	8 (50)	
51–60 years	11 (64.7)	6 (35.3)	0.185
Above 60 years	27 (40.3)	40 (59.7)	
Sex			
Male	22 (51.2)	21 (48.8)	0.368
Female	24 (42.1)	33 (57.9)	
Education			
Till secondary	28 (40)	42 (60)	0.066
Graduate or more	18 (60)	12 (40)	
Monthly income			
Less than Rs. 20,000/-	26 (44.8)	32 (55.2)	0.782
More than Rs. 20,000/-	20 (47.6)	22 (52.4)	
Occupation			
Unemployed	15 (41.7)	21 (58.3)	0.514
Employed/Retired	31 (48.4)	33 (51.6)	
Residence			
Rural	33 (47.1)	37 (52.9)	0.726
Urban	13 (43.3)	17 (56.7)	
Type of diabetic treatment			
Without insulin	29 (44.6)	36 (55.4)	0.705
With insulin	17 (48.6)	18 (51.4)	
Personal experience of hypoglycemia			
Yes	34 (54)	29 (46)	0.037#
No	12 (32.4)	25 (67.6)	
Family experienced hypoglycemia			
Yes	15 (53.6)	13 (46.4)	0.343
No	31 (43.1)	41 (56.9)	
Duration of diabetes			
< 10 years	21 (36.8)	36 (63.2)	0.034#
More than 10 years	25 (58.1)	18 (41.9)	
Source of information on hypoglycemia			
Treating Doctor	23 (65.7)	12 (34.3)	0.004#
Others	23 (35.4)	42 (64.6)	

# p< 0.05 - Factors significantly associated with good knowledge of hypoglycemia

The importance of timely medication intake and regular visits to the treating doctor was known to most patients with regard to the measures to prevent hypoglycemia. SMBG is a pillar of effective diabetes self-management aiding in prevention of hypoglycemia and in glycemic control. It helps in rightly modifying diet, exercise, and pharmacotherapy.[9] SMBG was known to less than half (40%) the patients and the hypoglycemia alert value (70 mg/dL) to even fewer (11%), in spite of a majority living with diabetes for more than 10 years. The need of approaching the doctor in the event of anticipated fasting and rigorous exercise was less known to the patients.

Most of the patients with good knowledge attributed it to their treating doctors and the association was also found to be statistically significant. It has been observed that health education imparted from either physician or nurse is better.[6] Moreover, these education and training programs are crucial for control of diabetes.[10] Surprisingly, only a handful (5%) of the patients reported social media as their source of knowledge on hypoglycemia. Use of social media to dissipate knowledge and in helping people with diabetes through interventions has proved beneficial.[11] Health institutions, clinicians, and other stakeholders who aim at improving the knowledge of diabetic patients on hypoglycemia should consider use of this method to spread awareness.

Although there is a great emphasis in diabetes self-management education[12] including various aspects such as diet, exercise, lifestyle modification, medication, and prevention of complications, a majority of participants predominantly residing in rural areas are still ill informed on the various aspects of hypoglycemia as noted in this study. This may be due to the fact that focus has shifted toward the pandemic during these times with the absence of regular follow-up visits and access to healthcare leading to the lack of reinforcement through health education and counseling sessions.[13] Ill-informed individuals may fail to recognize hypoglycemic episodes and repeated episodes of severe hypoglycemia can result in long-term cognitive dysfunction and even brain death.[14,15]

This study gives us an insight into the level of knowledge regarding various aspects of hypoglycemia – a potentially grave but preventable complication of diabetes, among patients presenting to the outpatient department of a tertiary care Medical College Hospital in central Kerala. It helps us in identifying and addressing aspects of the knowledge gap in relation to hypoglycemia. Treating doctors, being the main source of information on hypoglycemia should focus more on educating patients regarding the possible symptoms, precipitating factors, prevention, and complications that can occur due to the

condition. Counseling and distribution of educational pamphlets on hypoglycemia were undertaken as part of the study to minimize the risk of future episodes and thereby improve quality of life in these patients.

The limitation of the study is that it is hospital-based and the sample size was small.

CONCLUSION

Although awareness of remedial measures of hypoglycemia is seen to be very good, knowledge of other important aspects such as symptoms, precipitating factors, preventive measures, and complications is alarmingly lacking even in an educated group of patients. Health education on various aspects of hypoglycemia and reinforcement at every visit by the treating doctors and nurses is the need of the hour. Renewed effort using potent tools of information dissipation like social media and social networking platforms and other innovative strategies need to be considered in improving awareness and preventing hypoglycemia. Similar studies to assess the knowledge of different aspects of hypoglycemia among the general public can be conducted post-pandemic at the community level.

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Original Article

Pulmonary Manifestations of Rheumatoid Arthritis in Patients Attending a Tertiary Care Hospital of North East India: A Cross-sectional Study

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Abstract

Background: Rheumatoid arthritis (RA) is a chronic inflammatory, systemic disease that produces its most prominent manifestations in the dirhrodial joints. The most common form of the disease is demonstrated by symmetrical, destructive, and deforming polyarthritis affecting small and large synovial joints with associated systemic disturbances, in addition to a variety of extraarticular features and the presence of circulating antiglobulin antibodies (rheumatoid factor). One of the most common extra-articular manifestations of RA is pulmonary involvement that can be seen in 30% of the cases. It is associated with a high titer of rheumatoid factor and is the second leading cause of death first being the infection.

Aims and Objectives: The aims of this study were to study the pattern of lung changes in patients with RA and to assess the change in lung function with respect to duration of disease and joint deformity.

Materials and Methods: Pulmonary function test was done in 80 RA patients aged between 30 and 60 years, attending the PMR department over a period of 3 months using Spirometry – model SPM –A. Spirometry parameters recorded were forced vital capacity (FVC), forced expiratory volume in 1 s (FEV_1), FEV_1/FVC, FEF_{25-75}, PEFR, and MVV. Data were entered in computer using Microsoft Excel. Descriptive statistics and other suitable statistical tests like χ^2 test were used as per applicability. A $P < 0.05$ will be considered as significant.

Results: Out of 80 RA patients, 54% showed changes in pulmonary function. About 44% of them had restrictive and 10% had obstructive type of lung changes. Among the spirometric parameters, most of them had normal FEV1/FVC and decreased FVC.

Conclusion: Different pattern of pulmonary function abnormalities could be manifested in RA patients and the restrictive pattern being the most common feature. Spirometry can be indicated as a baseline assessment and for follow-up of RA patient for the early detection and timely management of the pulmonary involvement.

Key words: FEF_{25-75}, Forced expiratory volume in 1 s, Forced vital capacity, MVV, PEFR, Pulmonary function test, Rheumatoid arthritis

INTRODUCTION

Rheumatoid arthritis (RA) is a chronic inflammatory, systemic disease that produces its most prominent manifestations in the diarthrodial joints. The most common form of the disease is demonstrated by symmetrical, destructive, and deforming polyarthritis affecting small and large synovial joints with associated systemic disturbances, in addition to a variety of extra-articular features and the presence of circulating antiglobulin antibodies (rheumatoid factor). The disease has a global distribution and involves all ethnic groups. The prevalence varies from 0.3% to 1.5% worldwide; it is 2.5 times greater in females than in males.[1] Although it is more common in females, extra-articular manifestations of the disease are more common in males and are mostly is seen in the 25–55 year age group.[1] The measurements of disease activity include the duration of morning stiffness lasting at least 30 min that

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often improves gradually after physical activity, the patients assessment of pain (visual analog score), the patients global assessment of disease activity, the patients assessment of physical function (disability), and the acute phase reactant value, namely, erythrocyte sedimentations rate (ESR), C-reactive protein (CRP), and hemoglobin concentration (Hb%). Extra-articular manifestations of RA can emerge during the course of the disease and even before the onset of arthritis. Patients can experience alongside of joint deterioration and severe disability, decreased quality of life, and premature mortality.[2] The presence of comorbidities such as cardiovascular disease, cancer (specifically lymphoma and lymphoproliferative diseases, lung cancer, and melanomas), infections, depression, and gastrointestinal disease can deteriorate the disease condition.[3]

One of the most common extra-articular manifestations of RA is pulmonary involvement that can be seen in 30% of the cases.[4,5] It is associated with a high titer of rheumatoid factor and smoking. It is the second leading cause of death first being the infection. This may present as interstitial pneumonitis, fibrosis, pleural involvement, pulmonary nodule, bronchiolitis obliterans organizing pneumonia, arthritis associated with pulmonary hypertension, and involvements of small and large airways.[4,5] The majority of lung disease occurs within the first 5 years after the initial diagnosis and may be a presenting manifestation in 10–20% of patients. Pleural disease is common but, usually, asymptomatic; autopsy studies have reported pleural involvement in 50% of cases, with only 10% clinically detected.[4,5] Interstitial lung disease (ILD) in patients with RA usually has a poor prognosis. Early studies identified a high postmortem incidence of RA-ILD, and this was subsequently supported by high-resolution computed tomography (HRCT) which confirmed that up to 25% of RA patients had ILD.[3] Spirometry is an inexpensive, readily available tool for assessing the lung function and can be applied on a large scale. Studies employing spirometry have detected abnormalities, mainly obstructive and restrictive patterns, in approximately 30% of patients with RA. It is a simple test to measure static lung volumes at rest – slow (inspiratory or expiratory) vital capacity (SVC), forced vital capacity (FVC) – and dynamic volumes forced expiratory volume in 1 s (FEV1), and flow-volume loops. Understanding the pattern of pulmonary abnormalities and its early detection can improve the quality of life and reduce mortality rate in patients with RA. Hence, the study was taken up to assess the pattern of lung changes in patients with RA and to assess the change in lung function with respect to duration of disease and joint deformity.

Primary Objective

The primary objectives of this study were as follows:

- To estimate the pattern of lung changes in patients of RA.

Secondary Objective

The secondary objectives of this study were as follows:

1. To assess the change in lung function with respect to duration of disease
2. To ascertain any association with joint deformity and lung changes.

MATERIALS AND METHODS

A hospital-based cross-sectional study was done in 80 adult patients with RA attending the PMR department, AGMC and GBPH, Agartala. Ethical clearance was obtained from the Institutional Ethical Committee of AGMC and GBPH. The study subjects were evaluated by general history, clinical examination, blood reports, and chest X-rays. Study was conducted from November 2022 to January 2023.

Inclusion Criteria for Cases

The following criteria were included in the study:

1. Based on the 2010 ACR classification criteria for RA (A Score of ≥6 out of 10 is needed to define RA)[14]

A. Joint involvement	Score
1 large joint	0
2–10 large joint	1
1–3 small joint (with or without involvement of large joints)	2
4–10 small joint (with or without involvement of large joints)	3
>10 joints (at least 1 small joints)	5
B.Serology (at least 1 test is needed for classification)	
Negative RF and Negative ACPA	0
Low positive RF or low positive ACPA	2
High positive RF or high positive ACPA	3
C.Acute phase reactants (at least 1 test is needed for classification)	
Normal CRP and normal ESR	0
Abnormal CRP and abnormal ESR	1
D.Duration of symptoms	
<6 weeks	0
≥6 weeks	1

ESR: Erythrocyte sedimentations rate, CRP: C-reactive protein

2. Age group of 30–60 years of both sexes
3. All the patients were consuming at least one disease-modifying antirheumatic drugs
4. Patients having no cardiovascular and respiratory complaints
5. Co-operative and willing to participate in the study.

Exclusion Criteria

The following criteria were excluded from the study:

1. History of any pulmonary disease
2. Clinical or radiological evidence of lung disease
3. Clinical or ECG evidence of cardiac disease
4. History of smoking, alcoholism or pregnancy
5. Treatment with corticosteroids
6. Those who are not willing to participate in the study
7. Patients with mixed connective tissue disease.

Study Tools

1. Electronic Spirometer – Model SPM – A
2. HRCT
3. Sphygmomanometer
4. Stethoscope
5. Case study format.

Recording of Spirometry

The participants were made to relax and wear comfortable loose clothing. The participant sat comfortably and nose clip was applied on the nose. The spirette was kept in the mouth with the lips sealing around it and was instructed to breathe calmly and care was taken not to block or bite the spirette. They were asked to do tidal breathing and fill the lungs completely and then asked to exhale as hard and fast as possible until the lungs were completely empty and inhale as hard and fast as possible until the end of the test. All the tests were conducted according to the American Thoracic Society/European Respiratory Society guidelines in a quiet room in sitting position by the Spirometer SPM-A for 3 times at every 15 min interval and best of 3 was taken into account.

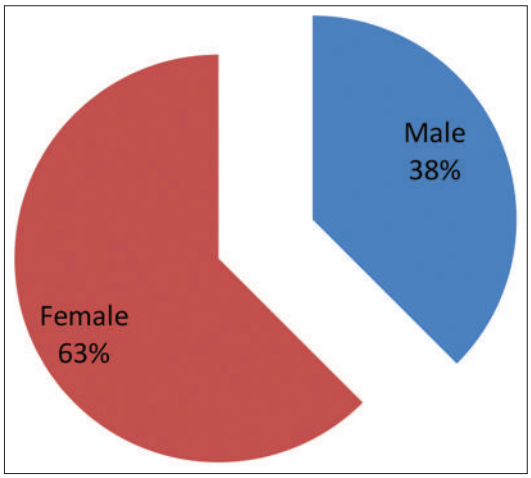

Figure 1: Gender-wise distribution of study participants

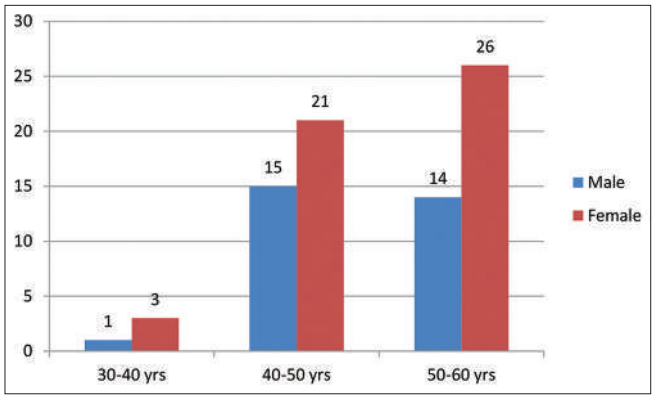

Figure 2: Age-wise distribution of patients

RESULTS

Data were entered in computer using Microsoft Excel. A $p < 0.05$ were considered as significant. A total of 80 RA patients had participated in this study. Among them, 62.5% were female and 37.5% were male, as shown in Figure 1. Mean age group was 43.24 ± 4.43 years. Age-wise distribution of study participants is shown in Figure 2. Mean duration of the disease was 7 ± 3.34 years. Disease duration of the study participants are shown in Figure 3. The lung function parameters interpreted were FVC, FEV_1, FEV_1/FVC, FEF_{25-75}, PEFR, and MVV which are shown in Figure 4 and Table 1. Changes in FVC ($P = 0.002$), FEV_1 ($P = 0.01$), and FEV_1/FVC ($P = 0.042$) were statistically significant. A significant negative correlation (r value = −0.239, $P = 0.053$) was found between FVC and duration of disease, as shown in Figures 5 and 6 which show the type of ventilatory defect in the study population. Figure 7 shows the frequency of presenting symptoms in RA patients. Figure 8 shows the result of rheumatoid factor tests in study group. Spirometric changes and its association with RA factor are shown in Figures 9 and 10 which show the laboratory investigation reports of CRP, ESR, and Hb% among the participants. The interpretation of X-rays among the study participants is shown in Figure 11.

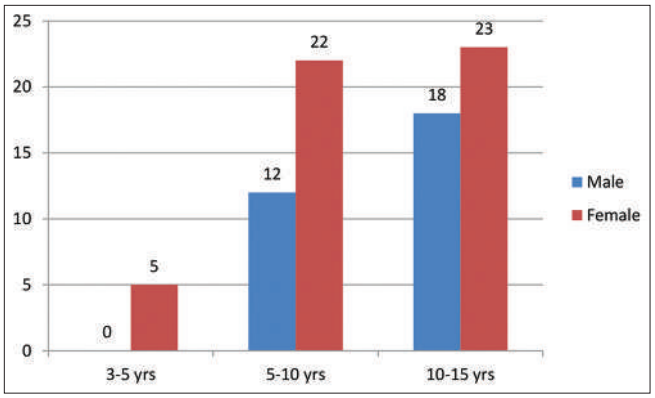

Figure 3: Disease duration of the study participants

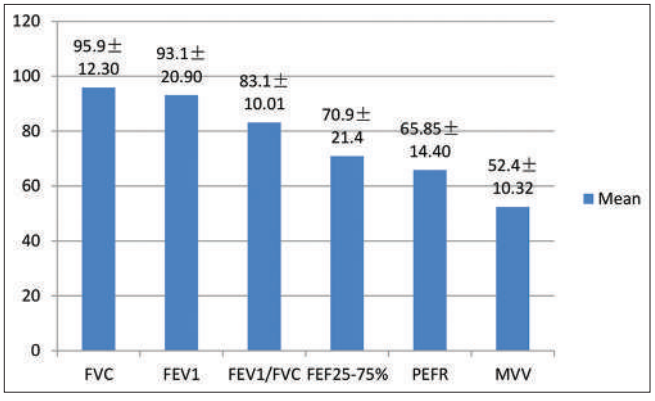

Figure 4: Mean ± Standard deviation of the spirometric parameters

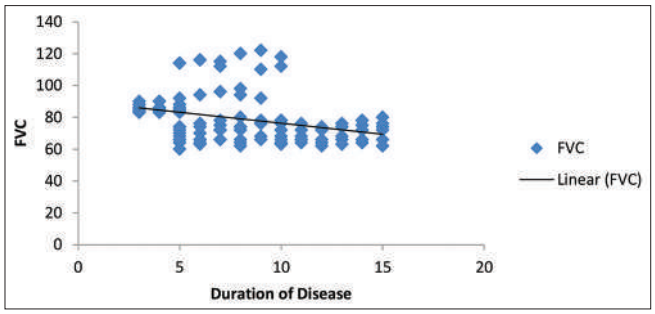

Figure 5: Correlation of forced vital capacity with duration of disease

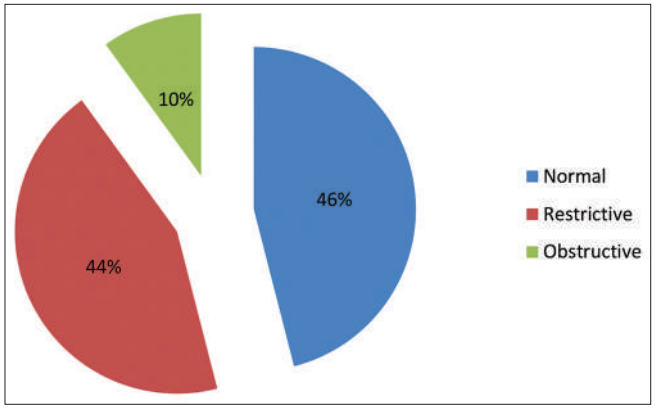

Figure 6: Ventilatory defect among the study subjects

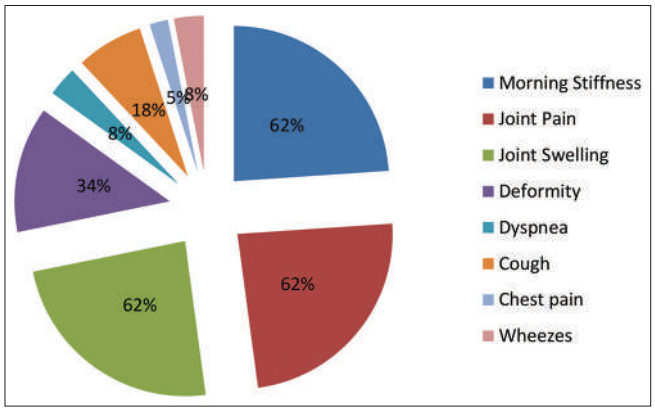

Figure 7: Frequency of presenting symptoms in rheumatoid arthritis patients

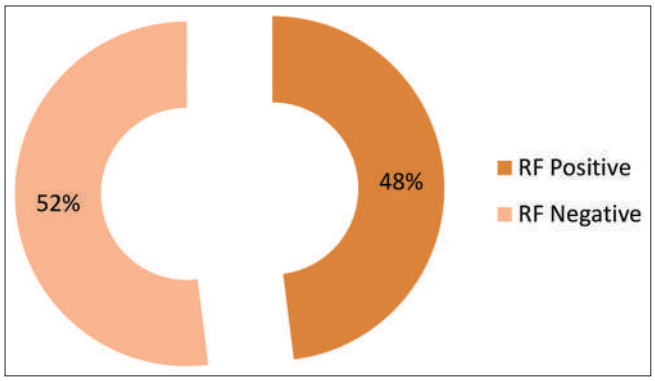

Figure 8: Rheumatoid factor test in the study participants

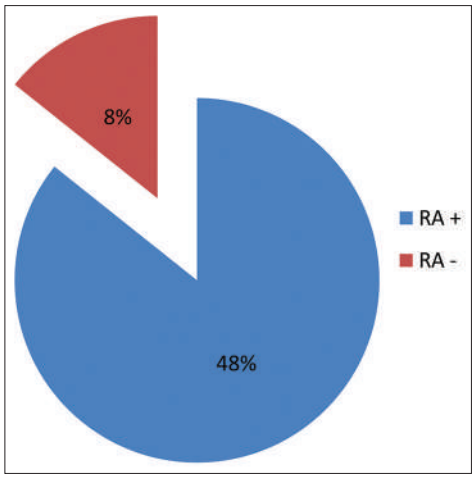

Figure 9: Spirometric changes and its association with rheumatoid arthritis factor

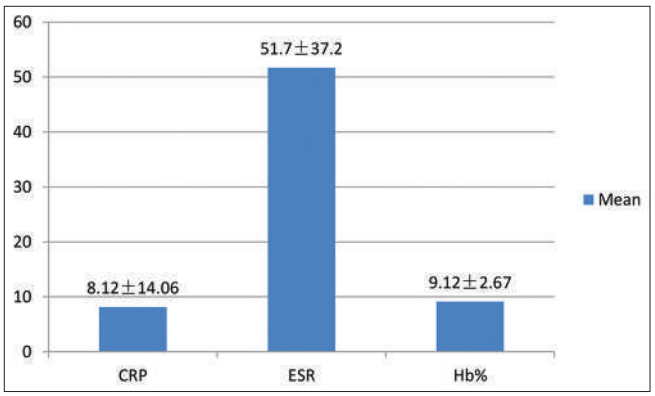

Figure 10: Other laboratory tests in study groups (C-reactive protein, erythrocyte sedimentations rate, and Hb%)

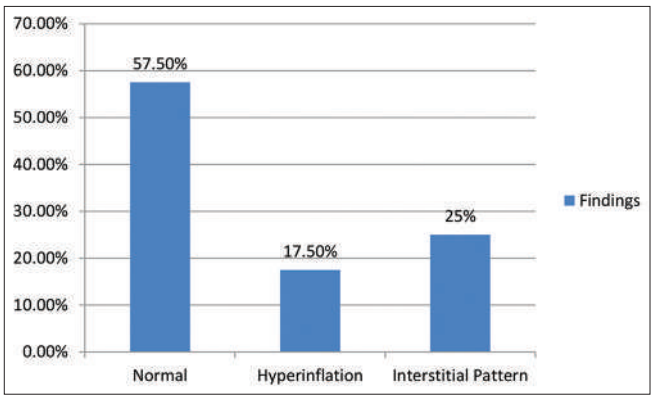

Figure 11: Interpretation of chest X-rays

DISCUSSION

RA is a chronic inflammatory, systemic disease involving mainly dirhrodial joints. One of the most common extra-articular manifestations of RA is pulmonary involvement. In our study, we assessed the pulmonary manifestations of RA using spirometry. Among the study population, 39% were male and 63% female. Mean age

Table 1: Spirometric parameters of the study participants

S. No.	Spirometric parameters	Mean±SD	*P*-value
1.	FVC	95.9±12.30	0.01*
2.	FEV1	93.1±20.90	0.002*
3.	FEV1/FVC	83.1±10.01	0.045*
4.	FEF 25–75%	70.9±21.4	1.26
5.	PEFR	65.85±14.40	0.45
6.	MVV	52.4±10.32	0.23

FEV1: Forced expiratory volume in 1 s, FVC: Forced vital capacity

group was 43.24 ± 4.43 years and the mean duration of the disease was 7 ± 2.23 years. The spirometry showed significant changes in FVC, FEV1, and FEV1/FVC and significant negative correlation of FVC with duration of the disease. The ventilatory defect pointed more toward the restrictive pattern. Interpretation of chest X-rays shows 57.5% normal, 17.5% hyperinflated, and 25% interstitial pattern.

The findings of our study are in association with the study of Ravikumar *et al*.[1] who concluded FVC, FEV1, FEV1/FVC, FEF 25–75%, and PEFR which were significantly decreased in patients with RA and 16% had obstructive and 28% had restrictive lung diseases. It is also in association with studies by Kalyani *et al*.[6] where they found restrictive ventilatory defect in 64% of rheumatoid patients with FEV1/FVC >70% and reduced vital capacity and total lung capacity. Obstructive ventilatory defect was seen in 10% of rheumatoid patients since FEV1/FVC <80% with increased residual volume and total lung capacity ratio. Remaining 26% of participants were normal. Lung parameters such as FVC, FEV1, FEV1/FVC, FEF 25–75%, and PEF were significantly lower in RA patients.

Fuld *et al*.[7] found that the prevalence of pulmonary function abnormalities was higher in asymptomatic rheumatoid patients when compared with the reference population. Avnon *et al*.[8] noted restrictive pulmonary abnormalities in 25.6% small airway disease in 14.6% and obstructive in 27%. Cortet *et al*.[9] and Radoux *et al*.[10] found that small airway obstruction is seen in 50% of cases with decrease in FEF 25–75%. Bilgici *et al*.[11] and Vergnenegre *et al*.[12] noted obstructive type of lung disease and reported a significant reduction in FEF 25–75%, FEV1/FVC. Devouassoux *et al*.[13] found that there is airflow obstruction with decreased FEV1/FVC and hyperinflation with increased residual volume and total lung capacity ratio. Findings of all these studies are in affirmation with findings of our study.

In our study, there was also significant negative correlation between FEV_1/FVC and duration of disease. Vergnenegre *et al*.[12] reported a significant negative relationship between FEF 25 and 75% and duration of articular disease in their study, whereas Cortet *et al*.,[9] Gabby *et al*.,[14] and Jamsshidi *et al*.,[15] found no relationship between disease duration and activity with PFT abnormalities in patients with RA.

In RA, restrictive ventilatory defect may be due to the activation of immune complexes in the alveolar walls. It results in the release of myeloperoxidase, collagenase, and elastase. There is destruction of lung tissue by phagocytosis and protease – anti-protease imbalance preventing the lung expansion and obstructive ventilator defect may be due to airway inflammation. Plasma immunoglobulin E level increases. Neuropeptides and chemokines are released from eosinophils, and mast cell damages the airway epithelium and causes hyper-responsiveness. This may result in partially reversible airway obstruction due to bronchial narrowing.

CONCLUSION

Lung is a potential target organ of the RA inflammatory disease process that can be manifested as different pattern of pulmonary function abnormalities. A restrictive pattern represents the most common feature. Spirometry can be indicated as a baseline assessment and for follow-up of RA patient for the early detection and timely management of the pulmonary involvement.

Limitations of the Present Study

The sample size in the present study is relatively small. Furthermore, unknown and subclinical complications, which are unaccounted for, may contribute to changes in lung function.

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Original Article

Fetomaternal Outcome of Pregnancies with Preterm Prelabor Rupture of Membranes

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Abstract

Background: Preterm premature rupture of membranes defines spontaneous rupture of fetal membranes before 37 completed weeks and before labor onset. Preterm premature rupture of membranes complicates approximately 3% of all birth but accounts for 30% of neonatal morbidity and mortality among premature gestations. It has been seen that in women with preterm prelabor rupture of membranes (PPROM), 50% will go in labor within 24–48 h and 70–90% within 7 days. Latency period is defined as interval between rupture of membranes and delivery.

Aims and Objectives: This study aimed to predict the fetomaternal outcome of pregnancies complicated by preterm premature rupture of membranes between 30 and 37 weeks of gestation.

Materials and Methods: We conducted a prospective observational study of women with singleton pregnancies who presented with rupture of membranes. A total of 65 women presenting with PPROM from 30 weeks were included in the study. The rupture of membranes was confirmed by per speculum examination. The period of gestation was confirmed by accurate dating or first-trimester ultrasound. Only low-risk patients were included in the study. Age of patient gestational age at presentation, latency period, mode of delivery, and maternal infection whether present or not were recorded. The patients were given antibiotics and corticosteroids during the latency period. Maternal infection was determined in terms of positive C-reactive protein and temperature of >100°C.

Results: Maternal outcome: Majority of the patients with PPROM belonged to the age group of 30–34 years (49.2%). Primigravidas were found to have increased chances of PPROM (56.9%). the gestational age of patients with PPROM was 32–33 weeks in 41.5%, followed by 30.8% in 30–31 weeks and ≥ 34 weeks in 27.7%. Majority of the patients (49.2%) delivered within 48 h of premature rupture of membranes. Maternal infection was found to be present in 38.5% of study patients. Urinary tract infection was present in 72.3% of patients. Majority of the patients delivered via vaginal route (58.5%). Fetal outcome: 61.5% of patients delivered babies with APGAR score >7.47.7% delivered babies of birth weight 1.5–2.4 kg. 55.4% of babies were admitted to NICU and 18.5% had respiratory distress syndrome (RDS). The overall perinatal mortality was 27.7% among the study group. 71.9% of those admitted to NICU, 43.8% of those with perinatal mortality, and 31.3% of those with RDS delivered within 48 h of admission.

Conclusion: Antenatal diagnosis to prevent PPROM by identifying the risk factors is an important tool in management. Steroids for fetal lung maturity, antibiotics to prevent fetal and maternal infection, and tocolytics can be given to delay delivery to reduce NICU admission.

Keywords: Preterm premature rupture of membranes, Latency period, Maternal infection, Preterm birth and neonatal outcome

INTRODUCTION

Preterm premature rupture of membranes is defined as spontaneous rupture of fetal membranes before 37 completed weeks and before labor onset. Preterm premature rupture of membranes complicates approximately 3% of all births but accounts for 30% of neonatal morbidity and mortality.[1,2] The main reason is thought to be prematurity and infections. The frequency of intra-amniotic infection in patients with preterm PROM in the absence of labor is 20–40%.[3,4-14] Premature rupture of membranes results from accelerated membrane weakening by various factors through an increase in local cytokines and an imbalance between metalloproteinase and increased protease and collagenase activity and factors that cause increased intrauterine pressure.[3] The various risk factors associated

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with preterm prelabor rupture of membranes (PPROM) are low socioeconomic status, smoking, genital tract infection, increasing intrauterine pressure, incompetent cervix, and others.[2] It has been seen that in women with PPROM, 50% will go in labor within 24–48 h and 70–90% within 7 days.[1] Latency period is defined as the interval between rupture of membranes and delivery.[1] Expectant management of PPROM includes the use of antibiotic treatment and steroids.[1] The basic aim of expectant management is to prolong the pregnancy for longer durations because of strong association between perinatal outcome and gestational age.

MATERIALS AND METHODS

A prospective observational study of 65 pregnant women, presenting with PPROM before 37-week gestation, was conducted in the year March–October 2022 at LDH, Srinagar, Kashmir. All patients with gestational age between 30 and 37 weeks with PPROM confirmed by ultrasound and clinical examination regardless of their age were included in the study. Exclusion criteria were all women with PPROM presenting before 30-week gestation; those with multiple gestations, preeclampsia, gestational diabetes, previous lower segment cesarean section (LSCS), or other types of preterm deliveries were excluded from the study. Detailed workup including history, general physical examination, abdomen and pelvic examination, and relevant specific investigations was noted. Gestational age was confirmed from the last menstrual period or dating scan. A sterile speculum examination was done and liquor draining from cervical os was observed for certain characteristics such as color and smell and cough test was done to confirm the rupture of membranes. High vaginal swab was taken and sent for culture sensitivity. All baseline investigations, CRP, and routine urine examination were done. All patients were given prophylactic antibiotics and steroid cover. Latency period, induction method, and mode of delivery were noted.

Soon after delivery APGAR score at 1 min and 5 min, birth weight, immediate complications, birth asphyxia, meconium aspiration, sepsis, and other complications were noted. Blood culture and sensitivity were taken in neonates. Neonatal sepsis was considered if blood culture was positive within the first 48 h of birth.

RESULTS

Maternal Outcome

Majority of the patients with PPROM belonged to the age group of 30–34 years [Table 1]. Primigravidas were found to have increased chances of PPROM (56.9%) as compared to multigravidas (43.1%) [Table 2]. The gestational age of patients with PPROM was 32–33 weeks in 41.5%, followed by 30.8% in 30–31 weeks and ≥34 weeks in 27.7% [Table 3]. 49.2% of the patients delivered in <48 h, 35.4% between 48 h–1 week, and 15.4% after 1 week [Table 4]. Maternal infection was found to be present in 38.5% of study patients [Table 5]. Urinary tract infection was present in 72.3% of patients [Table 6]. Majority of the patients delivered via vaginal route – 58.5% and 41.5% delivered through cesarean section [Table 7].

Fetal Outcome

61.5% of patients delivered babies with APGAR score >7and 38.5% with APGAR score <7. 47.7% delivered babies of birth weight 1.5–2.4 kg and 40% with >2.5 kg [Table 8]; 12.3 delivered <1.5 kg babies. 55.4% of babies were admitted to NICU and 10.8% had respiratory distress syndrome (RDS) [Table 8]. The overall perinatal mortality was 27.7% among the study group. 71.9% of those admitted to NICU, 43.8% of those with perinatal mortality, and 31.3% of those with RDS delivered within 48 h of premature rupture of membranes [Table 9].

Statistical Methods

The recorded data were compiled and entered in a spreadsheet (Microsoft Excel) and then exported to data editor of SPSS Version 20.0 (SPSS Inc., Chicago, Illinois, USA). Continuous variables were expressed as mean ± SD and categorical variables were summarized as frequencies and percentages. Graphically, the data were presented by bar and pie diagrams. Chi-square test or Fisher's exact test, whichever appropriate, was employed for comparison of neonatal complications according to latency period. $P < 0.05$ was considered statistically significant.

DISCUSSION

The present study entitled "Fetomaternal outcome in preterm premature rupture of membranes" is a prospective observational study done in Government Lalla Ded Hospital, Srinagar, between March and October 2022. A total of 65 patients were included in the study. PPROM or rupture of membranes before onset of labor is seen in 10% of all deliveries which makes the fetus and intrauterine contents more vulnerable to bacterial infection. It can lead to increased maternal complications neonatal morbidity and mortality.

In our study, cases were selected from all age groups. The mean age of patients with PPROM is 31.6 years which is comparable to the study conducted by Yasmin and Barakat where they found the average age of patients with PPROM to be 28.2 years.[15]

Table 1: Age distribution of study patients

Age (years)	Number	Percentage
25–29	19	29.2
30–34	32	49.2
≥35	14	21.5
Total	65	100

Mean±SD (range)=31.6±3.62 (25–40 years)

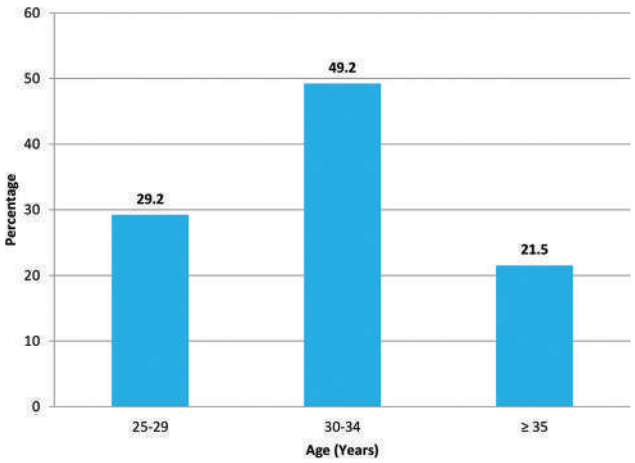
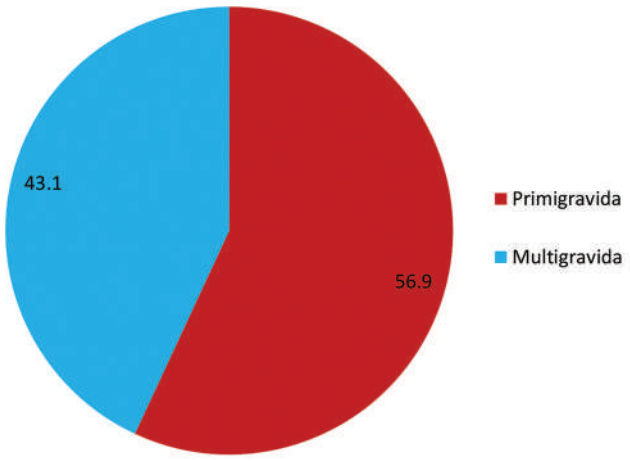


Table 2: Parity of study patients

Parity	Number	Percentage
Primigravida	37	56.9
Multigravida	28	43.1
Total	65	100



In our study, 56.9% of the study population were primigravidas. This finding correlates with a study of Akhtar *et al.* where 45% of women with PPROM were primigravidas.[16] Majority of the study patients had a gestational age of 32–33 weeks at presentation (41.6%) while 30% were <32 weeks of gestation. Adeniji and Atanda and Biswas *et al.* found that most of the patients with PPROM belonged to the gestational age of >36 weeks which is not comparable with our study.[17,18]

Table 3: Gestational age at admission among study patients

Gestational age (weeks)	Number	Percentage
30–31 weeks	20	30.8
32–33 weeks	27	41.5
≥34 weeks	18	27.7
Total	65	100

Mean±SD (range)=33.7±2.24 (20–36 weeks)

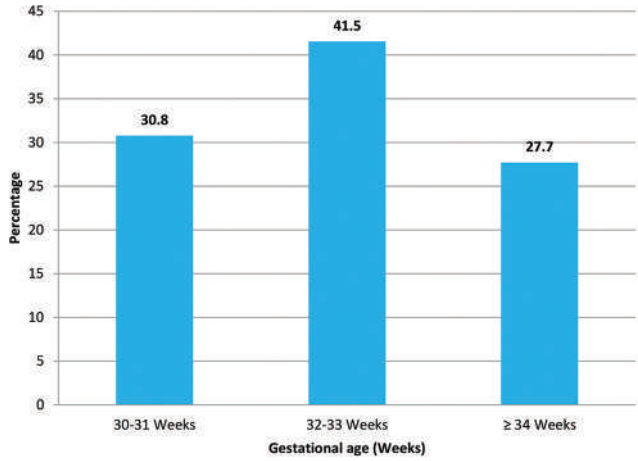
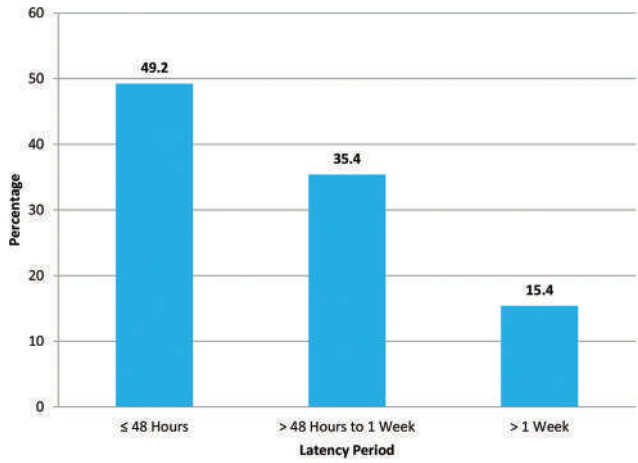


Table 4: Distribution of study patients as per latency period

Latency period	Number	Percentage
≤48 h	32	49.2
>48 h to 1 week	23	35.4
>1 week	10	15.4
Total	65	100



41.5% of patients in our study delivered via LSCS while 58.5% had normal vaginal delivery (VD). Tavassoli *et al.* in their study found 32% of patients with PPROM delivered through LSCS which is comparable with our study[19] Pasquier *et al.* also found the LSCS rate to be 58.7% in study patients which is also comparable to our study.[20] In

Table 5: Maternal infection in study patients

Maternal infection	Number	Percentage
Yes	25	38.5
No	40	61.5
Total	65	100

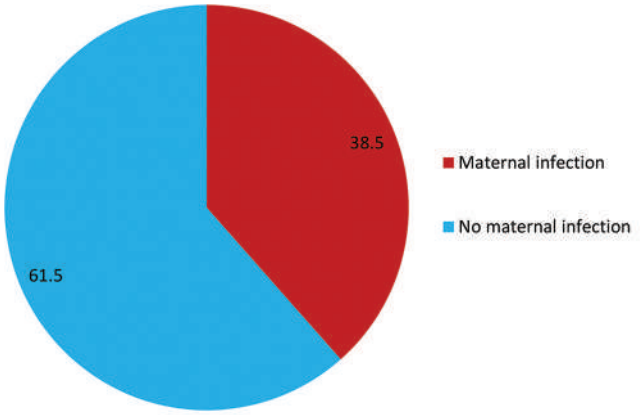


Table 6: Urine infection in study patients

Urine infection	Number	Percentage
Yes	47	72.3
No	18	27.7
Total	65	100

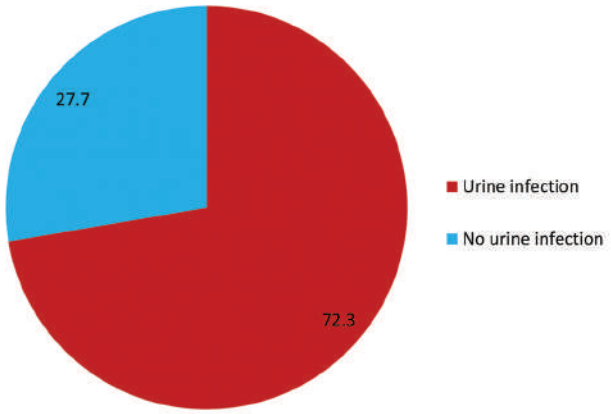


Table 7: Mode of delivery among study patients

Mode of delivery	Number	Percentage
Lower segment cesarean section	27	41.5
Vaginal delivery	38	58.5
Total	65	100

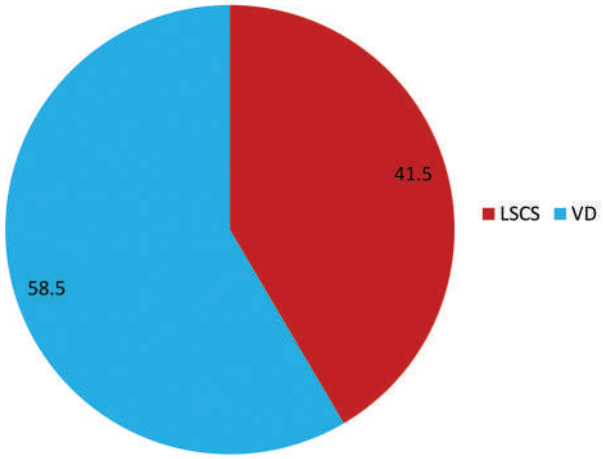
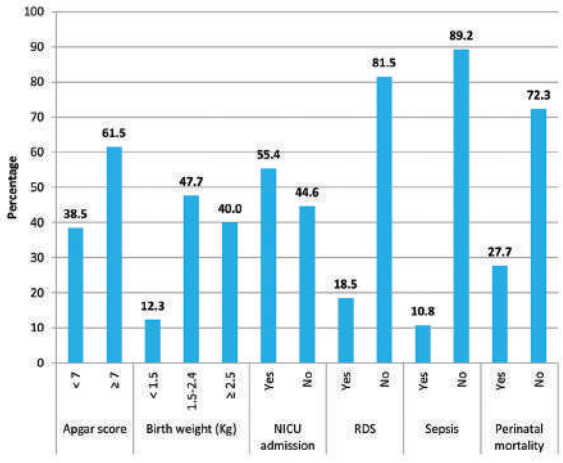


Table 8: Fetal outcome of study neonates

Parameter	Number	Percentage
APGAR score		
<7	25	38.5
≥7	40	61.5
Birth weight (kg)		
<1.5	8	12.3
1.5–2.4	31	47.7
≥2.5	26	40.0
NICU admission		
Yes	36	55.4
No	29	44.6
Respiratory distress syndrome		
Yes	12	18.5
No	53	81.5
Sepsis		
Yes	7	10.8
No	58	89.2
Perinatal mortality		
Yes	18	27.7
No	47	72.3



the study conducted by Tahir *et al*., only 14% of patients with PPROM delivered via LSCS while 86% delivered via normal VD which is not comparable with our study.[21] Eleje *et al*. and Ibishi and Isjanovska in their study found that only 23% and 28% of study patients delivered via LSCS, respectively. These findings were not comparable with our study.[22,23]

The incidence of maternal infection (clinical chorioamnionitis) in our study was 38.5% which is higher than the study conducted by Seo *et al*. where they found the maternal infection in 26.3% of PPROM.[24] The higher incidence could be attributed to multiple digital

Table 9: Neonatal complications according to latency period

Neonatal complications	Latency period						*P*-value
	≤48 h [*n*=32]		>48 h–1 week [*n*=23]		>1 week [*n*=10]		
	No.	% age	No.	% age	No.	% age	
Respiratory distress syndrome	10	31.3	2	8.7	0	0	0.027*
Sepsis	4	12.5	1	4.3	1	10	0.586
Perinatal mortality	14	43.8	3	13.0	1	10	0.017*
NICU admission	23	71.9	10	43.5	3	30	0.024*
APGAR score<7	15	46.9	8	34.8	2	20	0.282
Low birth weight	20	62.5	14	60.9	5	50	0.776

*Statistically significant difference (*P*<0.05)

examinations. The most important risk factor in PPROM in our study is urinary tract infection found in 71.2% of study patients. Begum *et al*. in their study found urinary tract infection in 33.33% of PPROM patients which is not comparable with our study.[25,26]

In our study among 65 cases, 18.5% born had RDS which is higher than the findings of Akter *et al*. where they found RDS in 8.16 of those born to mothers with PPROM.[27]. Perinatal mortality in our study was 27.7% which was higher than the study conducted by Tavassoli *et al*. where they found perinatal mortality in 8.8% of study patients.[19] This higher incidence could be attributed to the fact that most of the infants delivered within 48 h of rupture of membranes. In our study, the survival rate was 72.3% of study infants which is comparable to the study conducted by Moretti and Sibai who reported a survival rate of 50–70%.[28]

In our study, 47.7% had birth weight of 1.5–2.4 kg which is comparable to the study conducted by Adhikary *et al*. where they found that 45.83% of babies had birth weight of 1.5–2.4 kg[29]

In our study, APGAR score of >7 was present in 61.5% of babies delivered to mothers with PPROM which is comparable with the study conducted by Adhikary *et al*. where they found APGAR score of >7 in 54.16% of babies.[29]

CONCLUSION

Antenatal diagnosis to prevent PPROM by identifying the risk factors is an important tool in management. Steroids for fetal lung maturity, antibiotics to prevent fetal and maternal infection, and tocolytics can be given to delay delivery to reduce NICU admission.

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Original Article

Comparative Study of BIOS versus Mono-Therapy for Achieving Optimal Metabolic Health in Adults with Type 2 Diabetes: Decoding the Effectiveness of a Comprehensive and Multi-Interventional Diabetes Care Program

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Abstract

Background: Obesity is a growing concern worldwide and has become a major risk factor for many chronic diseases, including type 2 diabetes (T2D), cardiovascular disease, and certain types of cancer. T2D is a chronic metabolic disorder that occurs when the body becomes resistant to insulin or does not produce enough insulin, resulting in high blood sugar levels. T2D has been labeled as the fastest-growing health challenge of the 21st century, affecting millions of people worldwide. However, recent research has shown that T2D can be reversed through a comprehensive and systematic approach that focuses on lifestyle management, including nutrition, fitness, and stress reduction.

Materials and Methods: The study enrolled 132 participants with T2D between the ages of 20 and 45, who had an hemoglobin A1c (HbA1c) level of over 6.5%. In the basic input/output system (BIOS), participants were provided with personal medical doctors specializing in diabetes and health coaches to offer tailored nutrition, customized fitness routines, and relevant lifestyle modifications for a holistic approach to reversing T2D. The baseline and final measurements of HbA1c levels, fasting blood sugar, and weight were recorded after 90 days. To assess the effectiveness of BIOS, a control group of 56 individuals with T2D was managed using traditional pharmacotherapy and regular dietary advice but did not participate in the BIOS program.

Results: The study was conducted over 132 subjects for 90 days duration, the 56 subjects were on monotherapy and 76 subjects were part of the BIOS program, presented as mean ± standard deviation (mean ± SD). In the monotherapy group, it is observed that average reduction of HbA1C values by (0.33%), percentage glucose variability (GV%) by (2.06%), body fat percentage by (1.65%), and BMI by (1.46). At the same time, the BIOS group has shown higher reduction in subject's HbA1C values by (1.3016%), GV% by (7.68%), body fat percentage by (3.74%), and BMI by (2.23). This study indicated that there are significant comparative reduction in subject's HbA1C values by (0.962727%), GV% by (5.62%), body fat percentage by (2.0939%), and BMI by (0.77) with BIOS program when compared to monotherapy.

Conclusion: The findings indicate that a comprehensive and multi-interventional diabetes care program involving personalized nutrition, fitness, and lifestyle modification such as BIOS, help in significant and sustained improvements in HbA1c level, glycemic control, and weight loss in adults with T2D.

Key words: Type 2 diabetes, Nutrition, Fitness, Lifestyle modification, Hemoglobin A1c reduction, Time in range, Glucose variability %, Body mass index, BF%, Basic input/output system

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INTRODUCTION

According to the International Diabetes Federation (IDF), in 2017, 425 million people worldwide had diabetes, a number that is projected to rise to 550 million by 2030.[1] The American Diabetes Association (ADA) reported that in 2019, diabetes was the direct cause of

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1.5 million deaths and a significant contributor to many other illnesses.[2]

The diabetes epidemic is a major public health challenge and is placing a substantial burden on healthcare systems worldwide. Uncontrolled diabetes leads to higher doses of medications, increased hospital admissions, and higher mortality rates. To mitigate the impact of this epidemic, it is essential to understand the current state of diabetes and its associated morbidities and to develop strategies for improving outcomes in affected individuals.[3]

The primary focus of this study is to evaluate the role of continuous glucose monitoring (CGM) with BIOS Health software as a tool to provide feedback and accountability necessary to create sustainable behavioral changes in lifestyle associated with raising the Food IQ and improved glycemic control.

The ADA lifestyle management guidelines incorporate the use of CGM as a tool to enhance diabetes management and improve health outcomes. CGM provides individuals with real-time information about their glucose patterns, which can inform decisions about lifestyle changes.[4] By combining the use of CGM with healthy eating, physical activity, stress management, and other diabetes self-care behaviors, individuals with diabetes can effectively manage their condition and improve their overall health and well-being.[5] Several studies have shown that CGM use can lead to improved glycemic control, reduced hemoglobin A1c (HbA1c) levels, and reduced insulin requirements.[6] Furthermore, CGM use has been associated with increased awareness of glucose fluctuations, improved self-monitoring of blood glucose, and increased motivation for lifestyle changes. In turn, these changes can lead to lifestyle behavioral change. Individuals with diabetes can achieve improved health outcomes, reduced dependence on medications and surgical interventions, and improved quality of life.[7]

The metabolic score obtained from CGM metrics such as HbA1c, time in range (TIR), and glucose variability (GV%) is an important tool in managing diabetes. HbA1c, which reflects average blood glucose levels over the past 2–3 months, is widely used as an indicator of glycemic control in diabetes management.[8] TIR, which measures the amount of time spent in the target glucose range, provides a more detailed view of glucose fluctuations throughout the day.[9] GV%, which indicates the degree of glucose fluctuations, is a valuable tool for evaluating the impact of meal patterns, stress, and other factors on glucose control. By combining these metrics, a metabolic score can be generated that provides a comprehensive view of the patient's glycemic control and identifies areas for improvement in diabetes management.[10]

The ADA recommends that individuals with diabetes require sustainable behavioral change and support from healthcare providers and peers.[10] The ADA stresses the importance of a patient-centered approach that considers individual needs, psychosocial factors, and collaboration between health-care providers and support networks.[11-15] Thus we propose a comprehensive diabetes care program that supports the people with T2D to achieve diabetes reversal. We call this multi-interventional approach as basic input/output system (BIOS).

BIOS is a deep tech-enabled coach lead program with diabetes expert physicians and a specialized nutritionist and performance coaches generating highly personalized lifestyle interventions such as meal plans, progressive fitness plans, and behavioral modifications.

MATERIALS AND METHODS

Methodology for randomized observational retrospective study of a data-driven behavioral tool:

Study Design

A randomized observational retrospective study was conducted to determine the effectiveness of data-driven behavioral tool BIOS incorporating BIOS, a deep-technology CGM software in promoting lifestyle changes in comparison of monotherapy in diabetes management.

Participants

132 participants were recruited for the study, 76 for BIOS with at least 3 months of CGM, 56 in monotherapy with standard diabetic management.

Intervention Model

Participants were randomly assigned to either the intervention group: BIOS Wellness Program (receiving the data-driven behavioral tool) and the control group: Monotherapy (receiving standard care).

Data Collection

In the interventional group, 76 BIOS Participants completed a QOL questionnaire, a baseline assessment, which includes a CGM with deep glucose insights, and then be monitored for 3 months. During this time, participants will provide blood glucose levels, and track their food intake using the data-driven behavioral tool (for the intervention group). In control group, 56 individuals completed a QOL questionnaire and were in standard diabetes care with monotherapy ADA guidelines (for the control group).

Data Analysis

The collected data were analyzed to compare the differences between the intervention with BIOS and control groups in

terms of changes in food intake, body composition: Body mass index and body fat %, glucose insights: eHbA1c, time in range, and GV%. Descriptive statistics will be used to describe the sample, and inferential statistics will be used to determine the effectiveness of the data-driven behavioral tool.

Masking

To maintain the blinding of participants, their CGM records were de-identified.

Selection Criteria

- Type-2 diabetes
- The study followed (ADA) criteria HbA1c ≥ 6.5%
- Age group 20–45.
- Individuals looking for lifestyle changes.

Exclusion Criteria

The following criteria were excluded from the study:

- Type-1 diabetes
- Chronic metabolic disorders
- Age group >18 and <45.

BIOS

The program begins with recruitment, where 132 participants undergo, a baseline assessment with HbA1C levels, 76 diabetics were enrolled in BIOS intervention and 56 were in the monotherapy control group.

Each participant is then assigned a personal team of diabetes specialists, nutritionists, and fitness coaches who provide customized nutrition plans, progressive fitness programs, and behavioral modification support. Participants have unlimited access to their coaches through an app and via telephone and can receive on-demand doctor consultations for the duration of the program. The program will be monitored and evaluated regularly to assess its effectiveness in improving eHbA1c levels, and promoting weight loss and improved overall health. Data collected during the program will be analyzed to assess the impact of the intervention on participants. Overall, the BIOS program offers a unique and comprehensive approach to managing type 2 diabetes (T2D), combining technology, expert guidance, and coach-led support for a personalized and effective intervention.

Glucose Monitoring

Participant was provided with a Liber Pro CGM Diabetes Sensor from Abbott Diabetes Care, which was used to record their daily glucose profiles for a period of 14 days from the baseline assessment.

Body Composition Analysis

In this study, the Actofit Pro-Max body composition analyzer was used.

The study group's body fat percentage and BMI were measured before and after BIOS therapy, while the control group's body fat percentage and BMI were measured before and after metformin treatment. The data collected from both groups were statistically analyzed to compare changes in body composition before and after treatment.

Personalized Nutrition

Each participant is assigned a personal nutrition coach who conducts a comprehensive assessment of the individual's nutritional needs and creates a personalized meal plan that takes into consideration their lifestyle, resources, and food preferences.

Fitness Program

The goal for each participant was to achieve 10,000 steps/day, and those with no movement challenges were gradually given an additional 1000 steps to reach the goal.

Physician Intervention

Effective management of T2DM requires a patient-centered approach, including lifestyle modifications, pharmacotherapy, and regular monitoring of blood glucose levels.

Lifestyle Modifications

Personalized health coaches were assigned to the participants in the BIOS program, offering behavior change strategies and diabetes education through counseling to help them achieve positive health outcomes and improve their quality of life. The BIOS program is a person-centered approach that utilizes team-based care and technology to provide one-on-one guidance and personalized interventions. Participants interacted with their coaches through various modes, including chat, WhatsApp, voice, and video calls, which minimized the risk of non-adherence, poor insights, and unpredictable outcomes over the 3 month program.

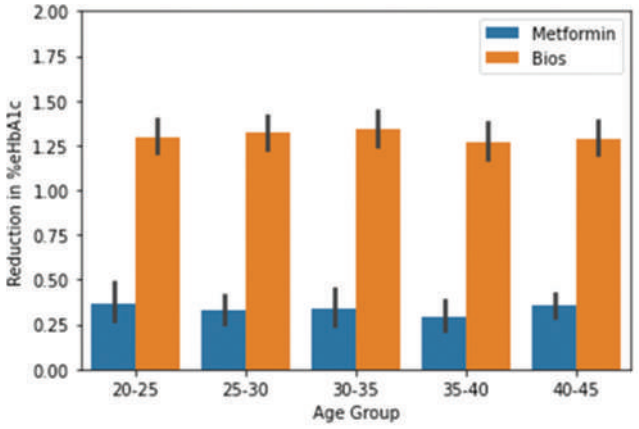
RESULTS

% eHbA1c

According to our study, treatment with BIOS resulted in a greater mean reduction in % eHbA1c levels (1.3 ± 0.2) compared to treatment with metformin control group (0.34 ± 0.16). Notably, participants in the age group between 30 and 35 years demonstrated a nearly 1% reduction in%eHbA1c levels when treated with Bios compared to Metformin. The mean reduction in % eHbA1c levels was less pronounced in other age groups, ranging from 0.93% to 0.99%.

GV%

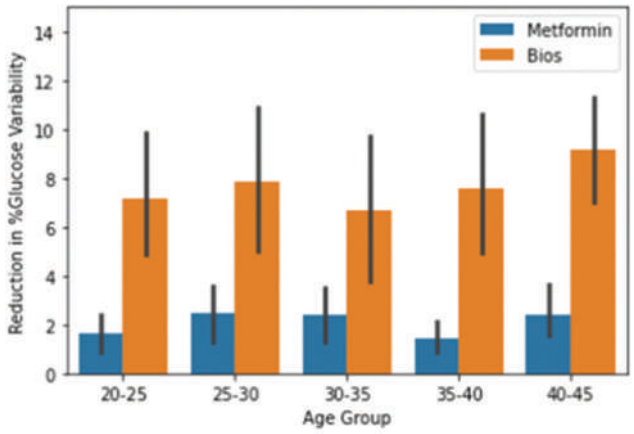
The study measured the mean reduction in GV% levels in the metformin control group and BIOS study group. GV% refers to the fluctuation of blood glucose levels over time.



The results showed that the mean reduction in GV% levels in the metformin control group was 2.05 ± 1.75, while the mean reduction in GV% levels in the BIOS study group was 7.66 ± 5.44. This indicates that BIOS treatment was significantly more effective in reducing GV% levels compared to metformin treatment.

The study also evaluated the impact of age on GV% reduction. The results showed that participants aged 40–45 years experienced a mean reduction of 6.724% in GV% levels when treated with BIOS compared to Metformin. However, other age groups showed lower mean reductions, such as 5.57% in 20–25, 5.4% in 25–30, 4.27% in 30–35, and 6.14% in 35–40 years.

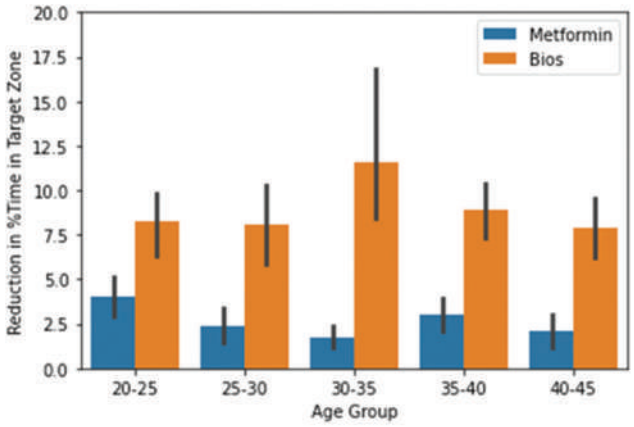
These findings suggest that Interventional BIOS treatment is significantly more effective at reducing GV% levels compared to mono-therapy, and the effectiveness may vary based on the patient's age. However, as with other outcomes such as % BMI and % body fat reduction, individual patient factors such as exercise and diet should also be considered when evaluating the effectiveness of these treatments in managing T2D.



% Time in Target Zone

According to our study, the mean reduction in % time in target zone levels when treated with metformin control group is 2.65 ± 1.77. However, the mean reduction in % time in target zone levels when treated with BIOS study group is 9.00 ± 5.68. Notably, participants in the age group between 30 and 35 years experienced the highest reduction in % time in target zone levels, with a drop of nearly 9.86% when treated with Bios compared to Metformin. On the other hand, other age groups exhibited a lesser mean reduction, such as 4.18% in 20–25, 5.68% in 25–30, 5.85% in 35–40, and 5.81% in 40–45 years.

Our findings are consistent with previous research that has demonstrated the effectiveness of Bios in improving glycemic control and reducing the % time in target zone levels in patients with diabetes. A systematic review and meta-analysis conducted by Liang *et al.*, reported a significant reduction in % time in target zone levels in patients treated with Bios compared to placebo or other glucose-lowering agents. Similarly, a randomized controlled trial by Ruan *et al.*, found that Bios treatment led to a greater reduction in % time in target zone levels compared to metformin in patients with T2D.



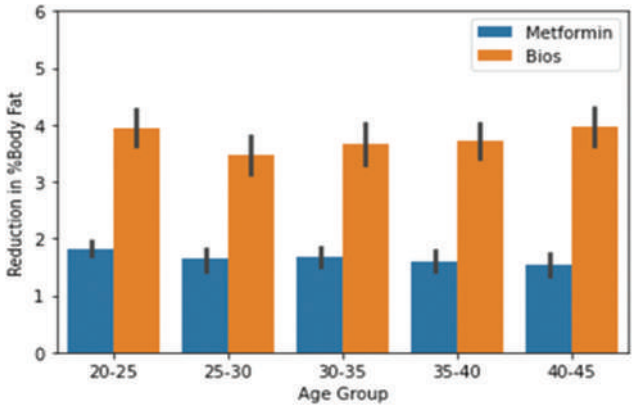
% Body Fat

The study measured the mean reduction in % body fat levels in the metformin control group and BIOS study group. % body fat refers to the percentage of body weight that is composed of fat.

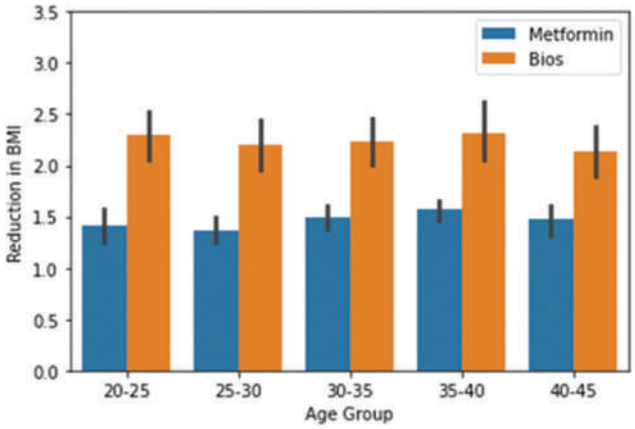
The results showed that the mean reduction in % body fat levels in the metformin control group was 1.65 ± 0.3, while the mean reduction in % body fat levels in the BIOS study group was 3.75 ± 0.71. This indicates that BIOS treatment was more effective in reducing % body fat levels compared to metformin treatment.

The study also evaluated the impact of age on % body fat reduction. The results showed that participants aged 40–45 years experienced a reduction of 2.43% in % body fat levels when treated with BIOS compared to metformin. However, a smaller mean reduction was observed in other age groups, including 2.11% in 20–25, 1.83% in 25–30, 1.99% in 30–35, and 2.11% in 35–40 years.

These findings suggest that BIOS treatment may be more effective in reducing % body fat levels compared to metformin treatment, and the effectiveness may vary based on the patient's age. However, as with % BMI reduction, individual patient factors such as exercise and diet should also be considered when evaluating the effectiveness of these treatments in managing obesity and related conditions.



Body Mass Index (BMI)



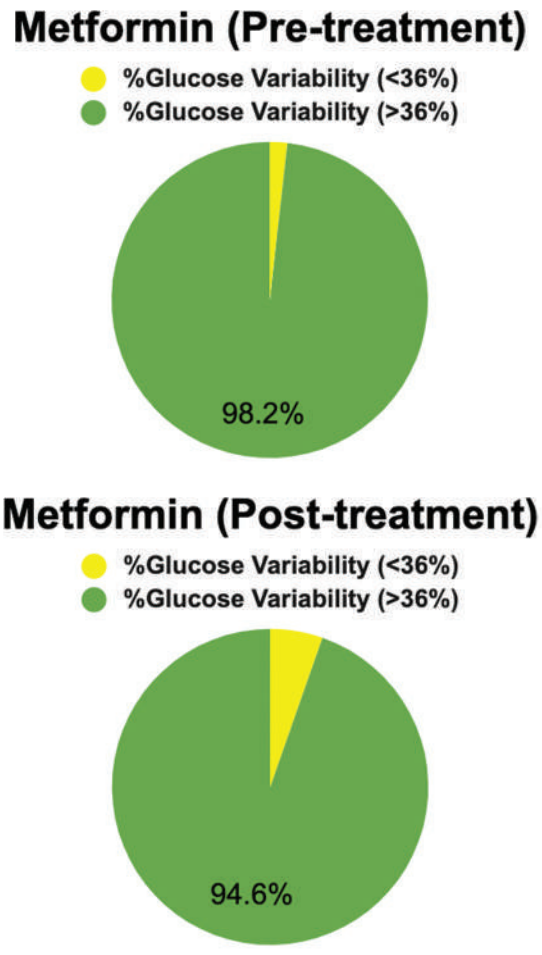
The study measured the mean reduction in % BMI levels following treatment with metformin in the control group and BIOS in the study group. % BMI refers to the percentage of body mass index, which is a measure of body fat based on height and weight.

The results of the study showed that the mean reduction in % BMI levels in the control group was 1.46 ± 0.24, while the mean reduction in % BMI levels in the BIOS study group was 2.23 ± 0.49. This indicates that the BIOS treatment was more effective in reducing % BMI levels compared to metformin treatment.

The study also looked at the impact of age on % BMI reduction. Among participants in the age group between 20 and 25 years, there was a reduction of 0.88% in % BMI levels when treated with metformin compared to BIOS. However, a smaller mean reduction was observed in other age groups, including 0.84% in 25–30, 0.74% in 30–35, 0.75% in 35–40, and 0.66% in 40–45 years.

These findings suggest that BIOS treatment may be more effective than metformin treatment in reducing % BMI levels, and the effectiveness may vary based on the patient's age. However, it's important to note that individual patient factors, such as diet and exercise, should also be considered when evaluating the effectiveness of these treatments in managing obesity and related conditions.

Monotherapy Group



The study found that treating patients with T2D using Monotherapy resulted in a significant increase in the number of patients whose GV% difference was <36%.

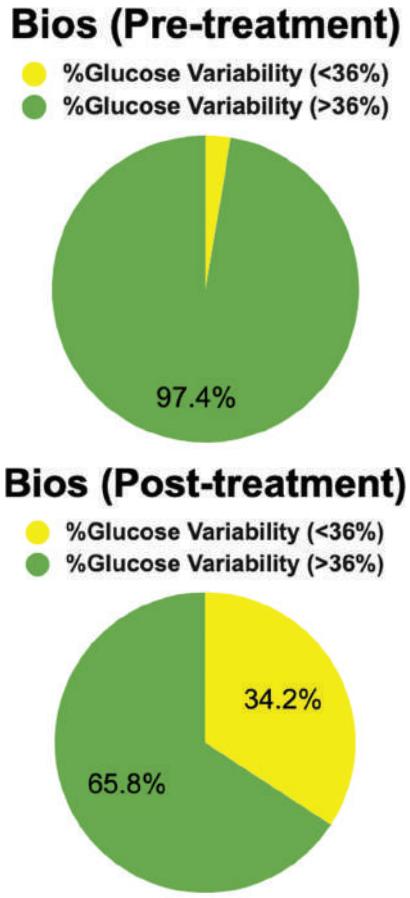
GV% refers to the amount by which a person's blood sugar level varies over a given period of time.

The study included two groups: The interventional group, which received monotherapy and BIOS treatment, and the control group, which received monotherapy treatment alone. Out of the 56 patients in the mono-therapy, only one patient achieved a reduction in GV% of <36% in Interventional BIOS. In contrast, out of the 56 patients in the mono-therapy group, three patients achieved this level of reduction when treated with metformin.

These results show that BIOS was more effective than the mono-therapy in reducing GV% in patients with T2D. These findings are consistent with previous research that has demonstrated the effectiveness of similar programs like BIOS in reducing GV in patients with T2D, as cited by the study authors.

The study adds to the existing body of evidence supporting the effectiveness of metformin in managing T2D. However, it's important to note that individual patient factors should be considered when deciding on the best treatment approach. In addition, more research is needed to determine the long-term effects of metformin treatment on managing T2D.

BIOS Group



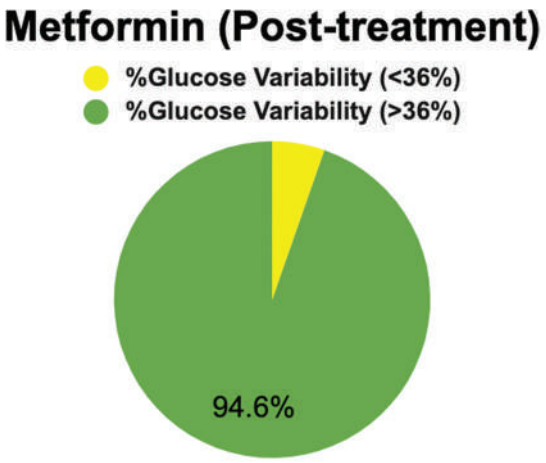
The study found that using BIOS as a treatment for patients with T2D resulted in a significant increase in the number of patients whose GV% difference was <36%. GV% refers to the amount by which a person's blood sugar level varies over a given period of time.

The study included two groups: The control group, which did not receive Metformin treatment, and the BIOS Group, which received BIOS treatment. Out of the 76 patients in the Control Group, only two patients achieved a reduction in GV% of <36% without Metformin treatment. In contrast, out of the 76 patients in the BIOS Group, 26 patients achieved this level of reduction when treated with BIOS.

These results show that BIOS was much more effective than the control group in reducing GV% in patients with T2D. The study suggests that BIOS could be a first-line treatment option for patients with T2D, especially those who are not responding well to other treatments or are unable to take Metformin.

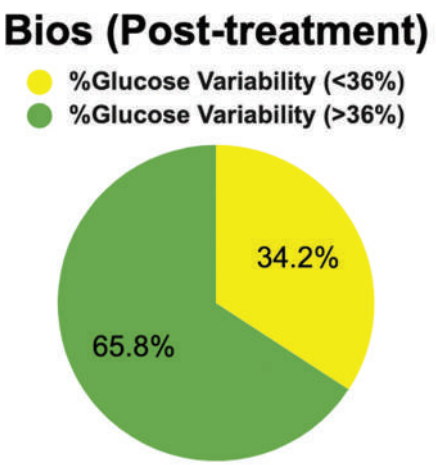
This study adds to the growing body of evidence supporting the use of BIOS as a first-line treatment for patients with T2D. However, it's important to note that more research is needed to determine the long-term effects of BIOS treatment on managing T2D. In addition, individual patient factors should be considered when deciding on the best treatment approach.

Interventional versus Control Group



The study found that treating patients with T2D using BIOS resulted in a significant increase in the number of patients achieving a reduction in GV% of <36%. GV% refers to the amount by which a person's blood sugar level varies over a given period of time.

The study involved two groups: The control group, which received mono-therapy treatment, and the BIOS group, which received BIOS + mono-therapy treatment.



The control group had only two patients who achieved a reduction in GV% of <36%, without the use of Metformin treatment. In contrast, 26 patients in the BIOS Group achieved this level of reduction when treated with BIOS.

This means that interventional BIOS was much more effective than the Control Group in reducing GV% in patients with T2D. The study suggests that BIOS could be a first-line treatment option for patients with T2D, especially those who are not responding well to other treatments or are unable to take Metformin.

It's important to note that this study provides evidence for the effectiveness of BIOS in reducing GV%, but more research is needed to determine its long-term effects on managing T2D. In addition, BIOS treatment may not be suitable for everyone, and individual patient factors should be considered when deciding on the best treatment approach.

DISCUSSION

The findings of this research paper demonstrate the efficacy of BIOS in improving glycemic control and reducing GV, time in target zone, body fat levels, and BMI levels in patients with diabetes compared to Metformin, a commonly used glucose-lowering agent.

The study found that treatment with Bios resulted in a greater mean reduction in %eHbA1c levels, indicating an improvement in overall glycemic control, compared to the Metformin control group. %eHbA1c is a marker of average blood glucose levels over the past 2–3 months. A reduction in %eHbA1c levels suggests that Bios was more effective in lowering blood glucose levels than Metformin. The reduction in %eHbA1c levels was particularly pronounced in the age group between 30 and 35 years, which demonstrated a nearly 1% reduction in %eHbA1c levels when treated with Bios compared to Metformin.

The study also found that Bios was superior to Metformin in reducing GV, as evidenced by a significantly higher mean reduction in GV% levels observed in the Bios study group compared to the Metformin control group. GV is a measure of how much blood glucose levels fluctuate over time. A reduction in GV% levels suggests that Bios was more effective in stabilizing blood glucose levels than Metformin. The age group of 40–45 years experienced the highest reduction in GV% levels when treated with Bios compared to Metformin.

Furthermore, treatment with Bios led to a greater reduction in % time in target zone levels compared to Metformin, indicating an improvement in glycemic stability. Time in target zone is a measure of how much time blood glucose levels are within a healthy range. A reduction in % time in target zone levels suggests that Bios was more effective in keeping blood glucose levels within a healthy range than Metformin. The age group between 30 and 35 years experienced the highest reduction in % time in target zone levels when treated with Bios.

In addition, the study found that treatment with Bios resulted in a greater reduction in body fat levels and BMI levels compared to Metformin. Body fat levels and BMI are measures of body composition and obesity. A reduction in body fat levels and BMI suggests that Bios was more effective in promoting weight loss than Metformin. However, the mean reduction in body fat and BMI was not significant in all age groups.

CONCLUSION

The findings of this research paper suggest that Interventional BIOS may be a more effective treatment option for patients with diabetes compared to Metformin. Bios was found to improve glycemic control, reduce GV, improve glycemic stability, and promote weight loss more effectively than Monotherapy. These findings may have important implications for the management of diabetes and the development of new treatment options. Further studies are needed to confirm these findings and explore the potential long-term effects of BIOS treatment in patients with diabetes.

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